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Filed Pursuant to Rule 424(b)(4)
Registration Nos. 333-201278 and 333-203298

PROSPECTUS

13,000,000 Shares

Carbylan Therapeutics, Inc.

Common Stock

$5.00 per share

This is the initial public offering of our common stock. Prior to this offering, there has been no public market for our common stock.

Our common stock has been approved for listing on The NASDAQ Global Market under the symbol "CBYL."

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012, and, as such, we have elected to take advantage of certain reduced reporting requirements for this prospectus and may elect to comply with certain reduced public company reporting requirements for future filings.

Investing in our common stock involves risks. See "Risk Factors" beginning on page 11.

	Per Share	Total
Initial Public Offering Price	$ 5.00	$65,000,000
Underwriting Discount and Commissions(1)	$ 0.35	$ 4,550,000
Proceeds to Carbylan (before expenses)	$ 4.65	$60,450,000

(1) We refer you to "Underwriting" beginning on page 143 for additional information regarding underwriting discounts, commissions and estimated offering expenses.

We have granted the underwriters an option to purchase up to 1,950,000 additional shares of common stock. The underwriters can exercise this right at any time within 30 days after the date of this prospectus.

Certain of our existing institutional investors, including investors affiliated with certain of our directors, have agreed to purchase an aggregate of 2,700,000 shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares to purchasers on or about April 14, 2015 through the book-entry facilities of The Depository Trust Company.

Leerink Partners

JMP Securities **Wedbush PacGrow Life Sciences**

April 8, 2015

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We are responsible for the information contained in this prospectus and in any free-writing prospectus we prepare or authorize. Neither we nor the underwriters have authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front of this prospectus.

Market, Industry and Other Data

This prospectus also contains estimates, projections and other information concerning our industry, our business and the markets for osteoarthritis treatments, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data are derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph are derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

Trademarks

This prospectus contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Summary

This summary highlights information contained in other parts of this prospectus. Because it is only a summary, it does not contain all of the information that you should consider before investing in shares of our common stock and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere in this prospectus. You should read the entire prospectus carefully, especially "Risk Factors" and our financial statements and the related notes, before deciding to buy shares of our common stock. Unless the context requires otherwise, references in this prospectus to "Carbylan Therapeutics," "we," "us" and "our" refer to Carbylan Therapeutics, Inc.

Overview

We are a clinical-stage specialty pharmaceutical company focused on the development and commercialization of novel and proprietary combination therapies that address significant unmet medical needs. Our initial focus is on the development of Hydros-TA, our proprietary, potentially best-in-class intra-articular, or IA, injectable product candidate to treat pain associated with osteoarthritis, or OA, of the knee. Current joint injection, or intra-articular, treatments for OA pain include corticosteroids, which provide short-term relief, and viscosupplements, which provide relief over the longer-term. In contrast, Hydros-TA utilizes our proprietary cross-linking technology to deliver both rapid pain relief with a low dose corticosteroid triamcinolone acetonide, or TA, and sustained pain relief from our novel hyaluronic acid viscosupplement. In our Phase 2b study of 98 patients, though not designed to show statistical significance, Hydros-TA demonstrated better pain reduction at all time points measured than Synvisc-One, the U.S. market-leading viscosupplement.

We are currently studying Hydros-TA in our COR1.1 trial, a Phase 3, multi-center, international, randomized, double-blind, three-arm trial enrolling up to 510 patients with grade two and grade three OA of the knee, comparing treatment with Hydros-TA to treatment with Hydros and with TA, on a standalone basis. As of March 31, 2015, approximately 350 subjects have been enrolled in COR1.1. We expect to initiate COR1.2, our second Phase 3 trial, open an investigational new drug application, or IND, and begin to enroll U.S. patients in COR1.2 in mid-2015. We anticipate reporting primary endpoint results from COR1.1 in early 2016 and COR1.2 by the end of 2016 and submitting our new drug application, or NDA, for Hydros-TA in early 2017. We believe that Hydros-TA will be well-positioned to become a leader in the OA injectable market, if we are able to demonstrate that Hydros-TA provides both rapid and sustained pain relief over a six month period.

We own the global development and commercialization rights to Hydros-TA, except in China, Taiwan, Hong Kong and Macau. We plan to commercialize Hydros-TA in the United States and, through partners, in the rest of the world. Following NDA approval in the United States, we expect to commercialize Hydros-TA using a small, 50 to 100 person specialty sales force targeting orthopedic surgeons, rheumatologists and pain specialists, the primary prescribers of IA steroids and viscosupplements. We have two issued U.S. patents and seven issued non-U.S. patents, the earliest of which will expire in 2030, and 18 patent applications worldwide covering our Hydros platform technology, including claims directed to composition of matter, methods of use and product-by-process.

Osteoarthritis Overview

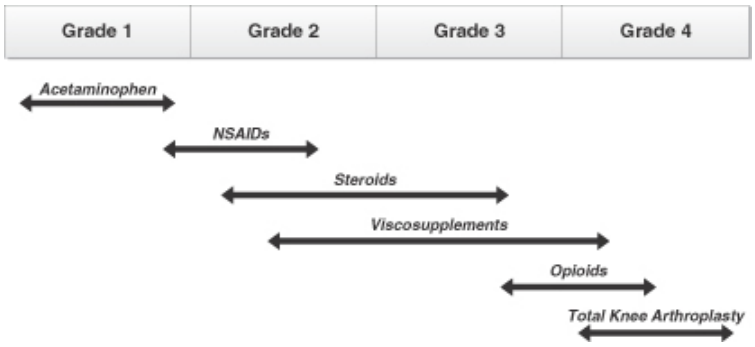
OA is a joint disorder involving the degradation of the IA cartilage, joint lining, ligaments and, ultimately, underlying bone. OA results in inflammation of the soft tissue and bony structures of the joint, which worsens over time and leads to progressive thinning of articular cartilage. Symptoms of this disease include pain, stiffness, swelling and limitation in the function of the joint. There is no known way to reverse the progression of OA and while there are a number of therapeutic options to treat the pain associated with OA, the disease typically continues to advance. We believe that the versatility provided by our proprietary cross-linking combination will

enable Hydros-TA to potentially address current shortcomings in the OA pain relief treatment spectrum for the knee, as well as address pain in other joints affected by OA, such as hip, shoulder, spine and ankle joints.

In the United States, there are over 27 million patients with OA, and approximately half of all adult patients will develop symptomatic OA of the knee. According to Millennium Research Group, in 2012, 1.65 million IA knee injections of hyaluronic acid, or HA, were administered. In the same year, worldwide sales of HA were approximately $1.76 billion, $726 million of which came from the United States.

Limitations of Current Treatments

OA severity is generally graded on a scale from one to four. When OA advances and oral or topical drug treatments are not sufficient to effectively address the associated pain, physicians often turn to IA treatments, such as corticosteroids, commonly known as steroids, and HA viscosupplements. While steroid injections can provide rapid pain relief, they generally provide only short-term pain relief of two to four weeks post injection. On the other hand, while HA injections can often provide long-term pain relief of up to approximately six months, they do not generally begin to provide peak pain relief until five weeks post injection. The following graph sets out what we believe to be the standard treatment progression for the treatment of OA pain in the knee:



Despite the use of currently available treatments, many OA patients experience persistent and worsening pain. Joint replacement surgery, often referred to as total knee arthroplasty, or TKA, is generally the last option for the treatment of OA. Compared to other treatments, this invasive surgery is an expensive option, with an initial surgical procedure cost of approximately $33,000 to $40,000. With patients receiving TKAs more frequently at a younger age, surgery to replace a previously performed TKA, known as a revision surgery, is increasingly common. Revision surgeries are not only more costly, at approximately $74,000, they are also associated with significantly higher morbidity and failure rates than the initial TKA surgery. Due to the expense of surgery and the limitations of treatments administered to prevent such surgeries, there exists a need for an alternative treatment that could provide both rapid and sustained relief from OA pain and potentially delay the need for joint replacement surgery.

Our Solution — Hydros-TA

Hydros-TA is a combination IA product, designed to provide both rapid and sustained pain relief with a single 6 ml intra-articular injection comprised of 52 mg of bacterially derived HA and 10 mg of TA. Rapid relief is provided from our low dose steroid component and sustained pain relief, up to six months, is provided from our proprietary HA component. Hydros-TA is comprised of bacterially derived HA-based hydrogel particles suspended in a solution of hyaluronic acid. The hydrogel particles contain the steroid, TA, which is entrapped within these particles. The dose of TA used in Hydros-TA is 10 mg, which is one quarter of the dose of TA that is often given clinically for

IA injections into the knee. We believe the incorporation of a low dose steroid into Hydros-TA provides a means of rapid pain relief currently missing from commercially-available HA. We believe that a clinically-proven and FDA-approved combination Hydros-TA product will provide a compelling alternative to sequential injections of steroids and viscosupplements.

Hydros-TA Clinical Program

Our completed Phase 2b clinical trial of Hydros-TA, known as COR1.0, was a prospective, multicenter, randomized, double-blind feasibility study to evaluate the safety and performance of Hydros-TA in subjects with OA of the knee. As is typical for OA clinical studies, our studies are designed using the Western Ontario and McMaster Universities Osteoarthritis Index, or WOMAC, which is a validated and accepted instrument developed to assess and quantify pain, joint stiffness and disability related to OA of the knee and hip. Our studies also utilize standardized criteria to define the number and percentage of defined positive "strict responders" (>50% and >20 mm improvements in WOMAC A (pain) or WOMAC C (function) scores, respectively, over baseline) in our clinical studies.

Our COR1.0 trial was conducted in eight clinical centers in Canada, Europe and the Caribbean with a total of 98 enrolled subjects that were treated and followed for six months thereafter. These subjects were randomized 1:1:1 to three study treatment arms: Hydros-TA, Hydros (the viscosupplement without steroid) and Synvisc-One (the U.S. market leading HA viscosupplement). In our primary endpoint, WOMAC pain score, pain reduction from baseline was observed in all treatment groups, however, Hydros-TA provided greater pain reduction compared to Synvisc-One at all study time points, as well as over the full study follow-up period of 26 weeks. Though we did not design our COR1.0 trial to enroll a sufficient number of patients to demonstrate statistical significance generally, the separation of pain reduction scores between Hydros-TA and Hydros was large enough to demonstrate statistical significance at the two week measurement point with the number of patients actually enrolled. Though statistical significance was not achieved at any other time point and in any other comparison of treatment arms, the separation between Hydros-TA and Synvisc-One represented approximately 10% of the baseline score, a numerical amount generally considered "clinically meaningful" and, we believe, not often seen in viscosupplementation trials with active comparators. For our secondary endpoints, WOMAC B (stiffness), WOMAC function, and responder rate, we saw a similar trend of improved outcomes with Hydros-TA compared to Synvisc-One. In addition, Hydros-TA was generally well-tolerated with fewer product-related adverse events reported than Synvisc-One.

The following table represents the COR1.0 trial baseline scores for each of the treatment groups, as well as the WOMAC pain score least square mean reductions from baseline over the full 26 week evaluation period, as well as at the 2, 6, 13 and 26 week time points post injection. The estimated difference between the treatment groups is also represented.

Time Point	Synvisc-One n=32	Hydros n=32	Hydros-TA n=34	Extra Pain Reduction Hydros vs. Synvisc-One	Extra Pain Reduction Hydros-TA vs. Hydros	Extra Pain Reduction Hydros-TA vs. Synvisc-One
Baseline	66.4	68.1	69.4	N/A	N/A	N/A
2 weeks	-28.5	-23.3	-35.6	5.2	-12.4	-7.2
6 weeks	-25.6	-32.4	-33.4	-6.7	-1.1	-7.8
13 weeks	-29.0	-33.9	-33.3	-4.9	0.6	-4.3
26 weeks	-28.9	-32.4	-35.2	-3.5	-2.8	-6.3
Overall	**-28.0**	**-30.5**	**-34.4**	**-2.5**	**-3.9**	**-6.4**

Since TA is an approved product in different pharmaceutical preparations, we will rely on the FDA's prior findings of safety and efficacy for TA and, thus, the Hydros-TA new drug application, or NDA, will benefit from

being filed under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or the FDCA, by eliminating the need for certain pre-clinical safety studies of TA. Hydros is considered a new molecular entity, or NME, and we are required to complete full pre-clinical testing to assure its safety profile. However, since Hydros-TA is our product candidate, not Hydros alone, in order to obtain regulatory approval of Hydros-TA, Hydros will not have to undergo any clinical testing independent of the Hydros-TA studies. We are required to complete two Phase 3 clinical trials and one safety trial in order to satisfy the requirements for the demonstration of safety and efficacy of Hydros-TA in our initial indication for OA pain in the knee.

We have designed and implemented our Hydros-TA Phase 3 program in close communication with the FDA. Based upon these discussions, we are enrolling our COR1.1 trial and preparing to enroll our COR1.2 trial, based upon the following study designs:

- *COR1.1:* The first of our two pivotal Phase 3 trials began enrollment in mid-January 2014. We are actively enrolling up to 510 subjects (of which approximately 350 patients have been enrolled as of March 31, 2015) at approximately 30 sites in Australia, Canada, New Zealand, Europe and the Caribbean. Subjects with OA grade two and grade three are randomized equally between three treatment arms: Hydros-TA, Hydros and TA. The objective of the trial is to demonstrate the safety and efficacy of Hydros-TA and the contribution of each of the two components in the Hydros-TA therapy. Our inclusion and exclusion criteria are designed to reduce the potential for placebo effect and to screen out non-responders where possible. The primary comparisons measure changes in pain under the WOMAC pain scale of Hydros-TA versus Hydros at two weeks and Hydros-TA versus TA at 26 weeks. Secondary endpoints include WOMAC function changes, subject and physician global assessment and responder rate. We expect top-line data from this trial in early 2016.

- *COR1.2:* The second of our two Phase 3 trials is scheduled to begin enrollment in mid-2015. We plan to enroll approximately 340 subjects at 20 to 30 sites in the United States, Australia, Canada and Europe. Subjects with OA grade two and grade three will be randomized equally between two treatment arms: Hydros-TA and TA. The objective of the trial will be to demonstrate the superiority of Hydros-TA compared to TA at 26 weeks post injection by measuring the change from baseline on the WOMAC pain scale. Secondary endpoints will include changes in WOMAC function, subject and physician global assessment and responder rate. We expect top-line data from this trial by the end of 2016.

- *COR1.3:* In addition to the COR1.1 and COR1.2 trials required for approval, we will need to collect safety data from an additional 400 to 450 patients, which will provide us with approximately 800 patients to make up our safety database. This trial will be conducted as a non-randomized, non-blinded trial. Patients who are screen failures for the COR1.1 and COR1.2 trials may be candidates for inclusion in this open-label trial.

Our Strategy

We intend to develop and commercialize novel and proprietary combination therapies for patients with osteoarthritis. The core principles of our strategy are to:

- ***Successfully complete our Phase 3 clinical trials for Hydros-TA and obtain FDA approval to market Hydros-TA.*** We are actively enrolling patients internationally in COR1.1, our first Phase 3 clinical trial of Hydros-TA for the treatment of OA pain in the knee. During meetings with the FDA, we addressed elements of our development plan for Hydros-TA and the FDA indicated that COR1.1 appears adequately designed to constitute a Phase 3 trial. We expect to initiate COR1.2, our second Phase 3 trial, open an IND and begin to enroll U.S. patients in COR1.2 in mid-2015. We anticipate reporting primary endpoint results from COR1.1 in early 2016 and COR1.2 by the end of 2016 and submitting our NDA for Hydros-TA in early 2017.

- ***Expand our Hydros-TA therapy to treat OA pain in additional joints.*** We believe Hydros-TA is a platform therapy for treating OA pain in multiple joints in the body. While our initial focus is on OA pain in the knee, we intend to use a portion of the proceeds of this offering to accelerate our development of Hydros-TA for the treatment of OA pain in the hip, shoulder, ankle, spine and other joints in the body. We do not believe that Hydros-TA will require reformulation to be used in additional joints affected by OA.
- ***Build commercial capabilities in the United States and selectively partner outside of the United States to maximize the value of Hydros-TA.*** We intend to commercialize Hydros-TA, if approved, in the United States through our own focused sales force of approximately 50 to 100 sales people, which we will build in connection with U.S. approval of Hydros-TA. We have partnered commercial rights for Hydros-TA in China, Taiwan, Hong Kong and Macau to Shanghai Jingfeng Pharmaceutical Co., Ltd. In other international markets, we intend to partner with established pharmaceutical companies to maximize the value of Hydros-TA without the substantial investment required to develop independent sales forces in those geographies.
- ***Utilize our strong management team's expertise to develop and commercialize Hydros-TA and other novel combination products.*** Our management team has extensive experience in designing and implementing efficient and effective drug development programs, and in building sales forces and bringing new therapies to market. We intend to maintain an organizational structure designed to allow us to cost-effectively advance our development and commercialization plans.

Risk Factors

Our business is subject to many risks and uncertainties of which you should be aware before you decide to invest in our common stock. These risks are discussed more fully under "Risk Factors" in this prospectus. Some of these risks include:

- we have incurred significant losses since our inception, and we expect to incur substantial losses for the foreseeable future and may never achieve or maintain profitability, which, among other things, raises substantial doubt about our ability to continue as a going concern;
- we have not generated any product revenue from, or received regulatory approval for, Hydros-TA or any other product candidate;
- we are substantially dependent on the success of Hydros-TA, which may not be successful in clinical trials, receive regulatory approval or be successfully commercialized, and we do not currently have any other product candidates in clinical development;
- we are a clinical-stage company and will require additional capital beyond this offering, including potentially prior to completing our Phase 3 clinical trials for, or commercializing, Hydros-TA;
- we have limited experience conducting clinical trials for Hydros-TA and may be unable to successfully enroll or complete clinical trials for, obtain regulatory approval for, or commercialize, Hydros-TA on the timeline we anticipate, or at all;
- we rely on third parties to manufacture and carry out the clinical trials of Hydros-TA, which could delay or limit future development or regulatory approval;

- we currently do not have the infrastructure to commercialize Hydros-TA, if it receives regulatory approval; and
- we may be unable to adequately maintain and protect our proprietary intellectual property assets, which could impair our commercial opportunities.

Implications of Being an Emerging Growth Company

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year following the fifth anniversary of the completion of this offering (December 31, 2020), (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.0 billion, (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30 and (4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. We refer to the Jumpstart Our Business Startup Act of 2012 herein as the "JOBS Act," and references herein to "emerging growth company" shall have the meaning associated with it in the JOBS Act.

Corporate and Other Information

We were originally incorporated in Delaware in March 2004 under the name Sentrx Surgical, Inc. We changed our name to Carbylan Biosurgery, Inc. in December 2005 and to Carbylan Therapeutics, Inc. in March 2014. Our principal executive offices are located at 3181 Porter Drive, Palo Alto, California, and our telephone number is (650) 855-6777. Our corporate website address is www.carbylan.com. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

The Offering

Common stock we are offering	13,000,000 shares
Common stock to be outstanding after this offering	24,246,963 shares
Option to purchase additional shares	1,950,000 shares
Use of proceeds	We intend to use the net proceeds from this offering to fund to completion both our ongoing COR1.1 and our future COR1.2 Phase 3 trials, for working capital and for other general corporate purposes. See “Use of Proceeds” on page 52 of this prospectus for more information.
Risk factors	You should read the “Risk Factors” section beginning on page 11 of this prospectus for a discussion of certain factors to consider carefully before deciding to purchase any shares of our common stock.
NASDAQ Global Market symbol	“CBYL”

The number of shares of our common stock to be outstanding after this offering is based on the shares of common stock outstanding as of December 31, 2014 and excludes the following:

- 1,328,873 shares of common stock issuable upon the exercise of outstanding stock options as of December 31, 2014, at a weighted average exercise price of $2.54 per share;
- 124,729 shares of common stock issuable upon the exercise of outstanding warrants as of December 31, 2014 at a weighted-average exercise price of $4.81 per share; and
- 1,155,897 shares of common stock reserved for future issuance under our 2015 equity incentive plan, or the 2015 Equity Plan (including 405,897 shares of common stock reserved for issuance under our previously existing 2014 stock option plan, or the 2014 Plan), which will become effective immediately prior to the closing of this offering, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under the 2015 Equity Plan.

Unless otherwise indicated, all information contained in this prospectus assumes:

- the automatic conversion of all our outstanding convertible preferred stock into an aggregate of 8,268,531 shares of common stock immediately prior to the closing of this offering;
- the conversion of all warrants exercisable for preferred stock into warrants exercisable for shares of our common stock immediately prior to the closing of this offering;
- the conversion of (i) our September 2014 convertible promissory notes and 184 days of accrued interest thereon into 1,281,505 shares of common stock and (ii) our February 2015 convertible promissory notes and 41 days of accrued interest thereon into 1,005,615 shares of common stock, each based on the initial public offering price of $5.00 per share, immediately prior to the closing of this offering;

- no exercise by the underwriters of their option to purchase up to an additional 1,950,000 shares of our common stock;
- the filing and effectiveness of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws immediately prior to the closing of this offering; and
- a 1-for-4 reverse stock split of our capital stock.

Participation in this Offering

Certain of our existing institutional investors, including investors affiliated with certain of our directors, have agreed to purchase an aggregate of 2,700,000 shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering.

Summary Financial Data

The following table summarizes certain of our financial data. We derived the statement of operations data for the years ended December 31, 2012, 2013 and 2014 and the balance sheet data as of December 31, 2014 from our audited financial statements and related notes appearing elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future. The summary financial data should be read together with our financial statements and related notes, "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" appearing elsewhere in this prospectus.

	Year Ended December 31,		
	2012	2013	2014
	(in thousands, except for share and per share amounts)		
Statement of Operations Data:			
License revenue	$ 1,538	$ 415	$ 29
Operating expenses:			
Research and development	1,959	4,229	8,294
General and administrative	1,412	1,402	3,412
Total operating expenses	3,371	5,631	11,706
Loss from operations	(1,833)	(5,216)	(11,677)
Other income (expense), net			
Interest income	1	2	2
Interest expense	(256)	(405)	(1,082)
Other income (expense), net	35	(59)	(602)
Total other income (expense)	(220)	(462)	(1,682)
Net loss	$ (2,053)	$ (5,678)	$ (13,359)
Net loss attributable to common stockholders	$ (2,164)	$ (5,678)	$ (13,359)
Net loss per share attributable to common stockholders, basic and diluted[1]	$ (5.14)	$ (13.42)	$ (21.81)
Weighted average common shares outstanding, basic and diluted[1]	421,152	423,059	612,525
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)[2]			$ (1.46)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)[2]			10,147,150

(1) See Note 2 to our financial statements appearing elsewhere in this prospectus for further details on the calculation of basic and diluted net loss per share attributable to common stockholders.

(2) The calculations for the unaudited pro forma net loss per share attributable to common stockholders, basic and diluted, assume: (i) the automatic conversion of all of our outstanding shares of convertible preferred stock into shares of our common stock, as if the conversion had occurred at January 1, 2014, or as of the issuance date of the convertible preferred stock, if later; (ii) the conversion of all of our warrants exercisable for convertible preferred stock into warrants exercisable for shares of our common stock; and (iii) the conversion of our September 2014 convertible promissory notes and 94 days of accrued interest thereon into 1,266,094 shares of common stock and the resulting loss on extinguishment of $2.5 million based on the initial public offering price of $5.00 per share. See Note 2 to our financial statements appearing elsewhere in this prospectus.

The table below presents our balance sheet data as of December 31, 2014:

- on an actual basis;
- on a pro forma basis, giving effect to (i) the automatic conversion of all our outstanding shares of convertible preferred stock into an aggregate of 8,268,531 shares of our common stock; and (ii) the conversion of all of our warrants exercisable for convertible preferred stock into warrants exercisable for shares of our common stock and the related reclassification of the preferred stock warrant liability to additional paid-in-capital, in each case, immediately prior to the closing of this offering; and (iii) the conversion of our September 2014 and February 2015 convertible promissory notes and 184 days and 41 days, respectively, of accrued interest thereon into 2,287,120 shares of common stock and the resulting loss on extinguishment of $3.6 million based on the initial public offering price of $5.00 per share, in each case, immediately prior to the closing of this offering; and
- on a pro forma as adjusted basis, giving further effect to the sale by us of 13,000,000 shares of our common stock in this offering at the initial public offering price of $5.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

	As of December 31, 2014		
	Actual	Pro Forma	Pro Forma As Adjusted
	(in thousands)		
Balance Sheet Data:			
Cash and cash equivalents	$ 3,897	$ 7,897	$ 64,947
Working capital	(2,506)	1,494	58,544
Total assets	6,644	10,644	67,694
Loans payable	4,435	4,435	4,435
Convertible promissory notes	2,131	—	—
Derivative liability	1,495	—	—
Preferred stock warrant liability	463	—	—
Convertible preferred stock	39,556	—	—
Accumulated deficit	(47,775)	(51,381)	(51,381)
Total stockholders' (deficit) equity	(44,181)	4,296	61,346

Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements

We have a limited operating history, have incurred significant losses since our inception and we will incur losses in the future. We have only one product candidate in clinical trials and no product sales, which, together with our limited operating history, makes it difficult to assess our future viability.

We are a clinical-stage specialty pharmaceutical company with a limited operating history. Pharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have focused substantially all of our efforts on our research and development activities on our lead product candidate, Hydros-TA. To date, we have not commercialized any products or generated any revenue from product sales. We are not profitable and have incurred losses in each year since our inception in 2004, and we do not know whether or when we will become profitable. We have only a limited operating history upon which you can evaluate our business and prospects. We continue to incur significant research and development and other expenses related to our ongoing operations. Our net losses for the years ended December 31, 2013 and 2014 were $5.7 million and $13.4 million, respectively. As of December 31, 2014, we had an accumulated deficit of $47.8 million. To date, we have financed our operations primarily through the sale of equity securities and debt facilities. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity and/or debt financings and strategic collaborations. We have not completed a pivotal clinical study for Hydros-TA and it will be several years, if ever, before Hydros-TA is ready for commercialization.

We will continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase significantly as we:

- continue our ongoing Phase 3 clinical trial of Hydros-TA and commence our second Phase 3 clinical trial of Hydros-TA;
- seek regulatory approvals for Hydros-TA;
- seek to expand the potential indications that we may treat with Hydros-TA, including performing preclinical studies and clinical trials evaluating the safety and effectiveness of Hydros-TA in treating OA in other joints;
- maintain, protect and expand our intellectual property portfolio;
- create additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;

- seek to discover and develop additional product candidates;
- acquire or in-license other product candidates and technologies; and
- attract and retain skilled personnel.

Our history of net losses and our expectation of future losses, together with our limited operating history, may make it difficult to evaluate our current business and predict our future performance. In addition, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

We have never generated any revenue from product sales and may never be profitable.

We have no products approved for sale and have never generated any revenue from product sales. Our ability to generate revenue from product sales and achieve profitability depends on our ability to successfully enroll and complete our clinical trials and obtain the regulatory and marketing approvals necessary to commercialize Hydros-TA. Even if we, or a collaboration partner, are successful in obtaining regulatory approvals to market Hydros-TA, our future revenue will depend upon many factors, including the size of any markets in which Hydros-TA has received approval, the accepted price for Hydros-TA, our ability to achieve sufficient market acceptance, reimbursement from third-party payors, the attractiveness of competing products and therapies, and whether we have royalty and/or co-promotion rights for that territory. We do not anticipate generating revenue from product sales until at least 2017 and may never realize any significant revenue from sales of Hydros-TA.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, which may include completing clinical trials of Hydros-TA, discovering additional product candidates, obtaining regulatory approval for such product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We may never succeed in these activities and, even if we do, may never generate revenue that is significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the Food and Drug Administration, or FDA, or comparable foreign regulatory bodies to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of Hydros-TA, or any future product candidates, our expenses could increase.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will require substantial additional financing to operate our business, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development or other operations.

Since our inception, substantially all of our resources have been dedicated to our research and development activities, including developing our lead product candidate, Hydros-TA. As of December 31, 2014, we had

working capital of $(2.5) million and capital resources consisting of cash and cash equivalents of $3.9 million. We believe that we will continue to expend substantial resources for the foreseeable future, including costs associated with research and development, conducting pre-clinical studies and clinical trials, obtaining regulatory approvals and sales and marketing. Because the outcome of any clinical trial and/or regulatory approval process is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development, regulatory approval process and commercialization of Hydros-TA.

The net proceeds from this offering will be approximately $57.1 million, based on the initial public offering price of $5.00 per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. Based on our current operating plan, we believe that our existing capital resources, along with the proceeds of this offering, will allow us to fund our operating plan through at least the next 12 months. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including, but not limited to:

- the progress, rate of enrollment, timing, scope, results and costs of our nonclinical and clinical trials for Hydros-TA, including the ability to enroll patients in a timely manner for clinical trials;
- the time and cost necessary to obtain regulatory approvals for Hydros-TA and the costs of post-marketing studies that could be required by regulatory authorities;
- our ability to successfully commercialize Hydros-TA;
- the manufacturing, selling and marketing costs associated with Hydros-TA, including the cost and timing of building our sales and marketing capabilities;
- our ability to establish and maintain collaboration partnerships, in-license/out-license or other similar arrangements and the financial terms of such agreements;
- the scope of our research and clinical development activities to expand the use of Hydros-TA for treating OA in other joints;
- the sales price and the availability of adequate third-party reimbursement for Hydros-TA;
- the cash requirements of any future acquisitions or discovery of future product candidates;
- the number and scope of nonclinical, pre-clinical and discovery programs that we decide to pursue or initiate;
- the time and cost necessary to respond to technological and market developments; and
- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of Hydros-TA or any other future product candidates.

Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate our research and development activities, clinical trials for Hydros-TA for which we retain such responsibility and our establishment and maintenance of sales and marketing capabilities or other activities that may be necessary to commercialize Hydros-TA.

Our independent registered public accounting firm has expressed doubt about our ability to continue as a going concern.

Based on our cash balances, recurring losses since inception and our existing capital resources to fund our planned operations for a twelve month period, our independent registered public accounting firm has included an explanatory paragraph in each of its reports on our financial statements as of and for the years ended December 31, 2014 and 2013 expressing substantial doubt about our ability to continue as a going concern. We will require significant additional funding to continue operations. If we are unable to continue as a going concern, we may be unable to meet our obligations under our existing debt facility, which could result in an acceleration of our obligation to repay all amounts thereunder, and we may be forced to liquidate our assets. In such a scenario, the values we receive for our assets in liquidation or dissolution could be significantly lower than the values reflected in our financial statements.

Risks Related to Our Business

We are substantially dependent on the success of our lead product candidate, Hydros-TA, which may not be successful in clinical trials, receive regulatory approval or be successfully commercialized.

To date, we have invested substantially all of our efforts and financial resources in the research and development of Hydros-TA, which is our lead product candidate and only product candidate in clinical trials. Hydros-TA is a new approach to treating osteoarthritis, or OA, pain in the knee by using a combination therapy treatment. Our near-term prospects, including our ability to finance our operations and generate revenue from product sales, will depend heavily on our ability to successfully develop, obtain regulatory approval for, and commercialize Hydros-TA. Our planned development, approval and commercialization of Hydros-TA may not be completed in a timely manner or at all. The clinical and commercial success of Hydros-TA will depend on a number of factors, many of which are beyond our control, including the following:

- the timely completion of the ongoing COR1.1 Phase 3 clinical trial and the initiation and timely completion of our planned COR1.2 Phase 3 clinical trial, both of which will depend substantially upon sufficient and timely patient enrollment, as well as the satisfactory performance of third-party contractors;
- whether Hydros-TA's safety and efficacy profile is satisfactory to the FDA to warrant marketing approval;
- whether FDA requires additional clinical trials prior to approval to market Hydros-TA;
- the timely receipt of necessary marketing approvals from the FDA;
- our ability to successfully commercialize Hydros-TA, if approved for marketing and sale by the FDA, including educating physicians and patients about the benefits, administration and use of Hydros-TA;
- achieving and maintaining compliance with all regulatory requirements applicable to Hydros-TA;
- the prevalence and severity of any side effects and overall safety profile of Hydros-TA and the acceptance of Hydros-TA as safe and effective by patients and the medical community;
- the availability, perceived advantages, relative cost, relative convenience and ease of administration, relative safety and relative efficacy of alternative and competing treatments;
- obtaining and sustaining an adequate level of coverage and reimbursement for Hydros-TA by third-party payors;
- the effectiveness of our marketing, sales and distribution strategy and operations and of those of any of our current or future collaborators;

- our ability, or any third-party manufacturer we contract with, to successfully scale up the manufacturing process for Hydros-TA, which has not yet been demonstrated, and to manufacture supplies of Hydros-TA and to develop, validate and maintain a commercially viable manufacturing process that is compliant with current good manufacturing practice, or cGMP, requirements;

- enforcing intellectual property rights;

- avoiding third-party interference, opposition, derivation or similar proceedings with respect to our patent rights, and avoiding other challenges to our patent rights and patent infringement claims; and

- a continued acceptable safety profile of Hydros-TA following approval.

Further, as of March 31, 2015, approximately 350 subjects have been enrolled in the COR1.1 Phase 3 clinical trial. Our completed COR1.0 study demonstrated a statistically significant result between Hydros-TA and Hydros at the two week time point, but statistical significance was not achieved at any other time point and in any other comparison of treatment arms. As such, previously unseen results may appear as we obtain results in our ongoing COR1.1 Phase 3 clinical trial and our future COR1.2 Phase 3 clinical trial. We have not yet filed an IND for Hydros-TA and will not be able to commence any clinical trials in the United States until we have submitted our IND filing and the FDA has not objected to our commencement of such trials. As such, we do not anticipate filing a new drug application, or NDA, with the FDA until early 2017.

If the number of patients in the market for Hydros-TA or the price that the market can bear is not as significant as we estimate, we may not generate significant revenue from sales of Hydros-TA, even if the above factors are overcome. Accordingly, we cannot assure you that Hydros-TA will ever be successfully commercialized or that we will ever generate revenue from sales of Hydros-TA. If we are not successful in completing the development of, obtaining approval for, and commercializing Hydros-TA, or are significantly delayed in doing so, our business will be materially harmed.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we may encounter substantial delays in our clinical studies. Furthermore, results of earlier studies and trials may not be predictive of future trial results.

Before obtaining marketing approval from regulatory authorities for the sale of Hydros-TA, we must conduct extensive clinical studies to demonstrate the safety and efficacy of Hydros-TA in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of pre-clinical and clinical studies of Hydros-TA may not be predictive of the results of later-stage clinical trials. For example, the positive results generated in our COR1.0 Phase 2b clinical study of Hydros-TA, which was not designed to enroll a sufficient number of patients to demonstrate statistical significance, do not ensure that the ongoing COR1.1 clinical trial, or future clinical trials, will demonstrate similar results. Hydros-TA may fail to show the desired safety and efficacy despite having progressed through pre-clinical studies and initial clinical trials. A number of companies in the pharmaceutical, biopharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for Hydros-TA.

We are actively enrolling patients internationally in our COR1.1 clinical trial, which is our first Phase 3 clinical trial of Hydros-TA, and we expect to initiate COR1.2, our second Phase 3 clinical trial of Hydros-TA, in mid-2015. However, we may experience delays in our ongoing COR1.1 or any other future clinical trials including COR1.2, and we do not know whether future clinical trials will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all.

Clinical trials can be delayed or terminated for a variety of reasons, including delay or failure to:

- obtain regulatory approval to commence a trial, if applicable;
- reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtain institutional review board, or IRB, approval at each site;
- recruit suitable patients in a timely manner to participate in our trials;
- have patients complete a trial or return for post-treatment follow-up;
- ensure that clinical sites observe trial protocol, comply with good clinical practices, or GCPs, or continue to participate in a trial;
- ensure adequate control of the clinical product handling and storage conditions;
- address any patient safety concerns that arise during the course of a trial;
- address any conflicts with new or existing laws or regulations;
- initiate or add a sufficient number of clinical trial sites; or
- manufacture sufficient quantities of Hydros-TA for use in our COR1.1 and COR1.2 trials or other future clinical trials.

Patient enrollment is a significant factor in the timing of clinical trials and is affected by many factors, including, in respect of our COR1.1 and COR1.2 trials, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by an independent data safety monitoring board, or DSMB, for such trial or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

If there are delays in the completion of, or termination of, any clinical trial of Hydros-TA, the commercial prospects of Hydros-TA may be harmed, and our ability to generate revenue from product sales will be delayed. In addition, any delays in completing the clinical trials will increase costs, slow down the development and approval process of Hydros-TA and jeopardize the ability to commence product sales and generate revenue from product sales. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of Hydros-TA.

Conducting our COR1.1 and a portion of our COR1.2 clinical trials in foreign countries present risks that may delay the completion of COR1.1 and COR1.2.

Conducting our COR1.1 and a portion of our COR1.2 clinical trials in foreign countries presents risks that may delay completion of these clinical trials. Such risks include the failure of physicians or enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes and political and economic risks relevant to such foreign countries. In addition, the FDA may determine that the clinical trial results obtained in foreign subjects are inadequate to support an NDA approval in the United States.

We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize Hydros-TA.

We do not have the ability to independently conduct clinical trials. We currently, and will continue to, rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct our clinical trials of Hydros-TA. The third parties with whom we contract for execution of the clinical trials we are conducting play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, these third parties are not our employees, and except for contractual duties and obligations, we control only certain aspects of their activities and have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely, and will continue to rely, on third parties to conduct our clinical trials, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with current GCPs for clinical studies. GCPs are regulations and guidelines enforced by the FDA through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our third-party contractors fail to comply with applicable regulatory requirements, including GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and increase cost.

Our product candidates may cause undesirable side effects or have other properties that could delay our clinical trials, or delay or prevent regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following regulatory approval, if any. If any of our product candidates receives marketing approval and we or others later identify undesirable side effects caused by the product candidate, the ability to market such product candidate could be compromised.

Undesirable side effects caused by a product candidate could cause us or regulatory authorities to interrupt, delay or halt clinical trials of the product candidate, result in the delay or denial of regulatory approval by the FDA or limit the commercial profile of an approved label. Some examples of drug-related side effects experienced by patients treated with Hydros-TA include injection site pain, arthralgia and injection site warmth. In the event that trials conducted by us of Hydros-TA or of future product candidates reveal an unacceptable severity and prevalence of these or other side effects, such trials could be suspended or terminated and the FDA could order us to cease further development of or deny approval of Hydros-TA, or any future product candidate, for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

In addition, in the event that Hydros-TA or any future product candidates receive regulatory approval and we or others later identify undesirable side effects caused by the product, a number of potentially significant negative consequences could occur, including:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or our collaboration partners, may be required to recall the product;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof, including the imposition of a Risk Evaluation and Mitigation Strategies, or REMS, plan that may require creation of a Medication Guide outlining the risks of such side effects for distribution to patients, as well as elements to assure safe use of the product, such as a patient registry and training and certification of prescribers;
- we, or our collaboration partners, may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us or a collaboration partner from achieving or maintaining market acceptance of a particular product candidate, if approved, and could result in the loss of significant revenue to us, which would materially and adversely affect our results of operations and business.

If we are unable to differentiate Hydros-TA from steroid injections, viscosupplements or other combination therapies for the treatment of OA pain, the ability to successfully commercialize Hydros-TA would be adversely affected.

Currently available steroid injections are effective at providing pain relief within a couple of days, but they do not last for more than two to four weeks and can have a damaging effect on the healthy cartilage. Most of these steroid injections are interchangeable with the choice usually stemming from cost to the patient and physician preference. These generic steroids also have well-established market positions and familiarity with physicians, healthcare payors and patients. There are five multi-injection viscosupplements (Hyalgan, Orthovisc, Supartz, Synvisc and Euflexxa) and three single-injection products (Synvisc-One, Gel-One and Monovisc) that are currently on the market, many of which are produced by large biopharmaceutical or pharmaceutical companies that have significant resources that they can devote to the development and promotion of their drug products. Of these viscosupplements, Synvisc-One represents over 50% of the U.S. viscosupplement market. Moreover, we believe that in at least some cases patients are treated with both a steroid injection and a viscosupplement injection within a relatively short proximity with an aim to achieve both rapid and sustained pain relief.

In addition to steroid injections and viscosupplements there are also a number of combination viscosupplement/steroid therapies currently in development. To our knowledge the most advanced of these candidates is currently in Phase 3 trials. To the extent that any of these therapies receive approval prior to Hydros-TA these competitors will have a first-mover advantage over us and, as such, will have the ability to begin developing brand recognition and customer loyalty that will increase the barriers that we will be required to overcome in order to gain commercial success.

Although we believe Hydros-TA has the potential for clinically meaningful differentiation in sustained pain relief as compared to currently available steroid injections and rapid pain relief as compared to viscosupplements, as clinical development of Hydros-TA advances and we receive data from additional clinical trials, it is possible that the data will not support such differentiation, which would adversely affect our ability to successfully commercialize Hydros-TA. Further, our ability to achieve commercial success will, at least in part, depend on our ability to differentiate ourselves from these existing therapies in such a way that physicians and patients will be willing to switch from existing therapies with which they are familiar to Hydros-TA. Once physicians incorporate a particular treatment into their practice they may not alter their practice absent compelling clinical evidence of safety and/or effectiveness and/or significant pricing reimbursement advantages.

If the FDA or other applicable regulatory authorities approve generic products that compete with Hydros-TA, the ability to successfully commercialize Hydros-TA would be adversely affected.

The FDA or other applicable regulatory authorities may approve generic products that could compete with Hydros-TA. Once an NDA, including a Section 505(b)(2) application, is approved, the product covered thereby becomes a "listed drug" which can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. The FDCA, FDA regulations and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for generic substitutes. These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredient, dosage form, strength, route of administration and conditions of use, or labeling, as Hydros-TA and that the generic product is bioequivalent to ours, meaning it is absorbed in the body at the same rate and to the same extent as Hydros-TA. These generic equivalents, which must meet the same quality standards as branded pharmaceuticals, would be significantly less costly than ours to bring to market and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product is typically lost to the generic product. Accordingly, competition from generic equivalents to Hydros-TA would materially adversely impact our ability to successfully commercialize Hydros-TA.

We face substantial competition and our competitors may discover, develop or commercialize products faster or more successfully than us.

The pharmaceutical, biotechnology and specialty pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. In addition, the competition in the OA pain market is intense. We have competitors in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions. In addition, we expect that injectable therapies such as Hydros-TA will continue to be used primarily after oral medications no longer provide adequate pain relief.

It is possible that our competitors will be able to leverage their large market share (for example, Sanofi S.A., the developer of Synvisc-One, holds more than 50% of the viscosupplement market as of 2012) to set prices at a level below that which is profitable for us. Our competitors may also be able to develop and market drugs or other treatments that are less expensive and more effective than Hydros-TA, or that will render Hydros-TA obsolete. It is also possible that our competitors will commercialize competing drugs or treatments before we can commercialize Hydros-TA. We also anticipate that we will face increased competition in the future as new companies enter into our target markets.

In addition to competitors in the viscosupplement market, as a result of the 2013 clinical practice guidelines released by the American Association of Orthopedic Surgeons, or AAOS, clinicians have been searching for alternatives to hyaluronic acid, or HA. To the extent additional alternative therapies are developed and receive positive support from AAOS, other professional medical societies and governmental agencies, these therapies would compete with Hydros-TA, if approved. For additional information regarding the AAOS guidelines, see the

risk factor below "—Third-party payor coverage and reimbursement status of newly-approved products is uncertain and such coverage for viscosupplementation may be hampered by recommendations from AAOS. Failure to obtain or maintain adequate coverage and reimbursement for Hydros-TA, if approved, could limit our ability to market Hydros-TA and decrease our ability to generate revenue."

Many of our competitors have materially greater name recognition and financial, manufacturing, marketing, research and drug development resources than we do, as well as a significant share of the existing market for OA pain treatments. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Large pharmaceutical companies in particular have extensive expertise in pre-clinical and clinical testing and in obtaining regulatory approvals for drugs. In addition, academic institutions, government agencies and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaboration partnerships or licensing relationships with our competitors.

For additional information regarding the competitive landscape for Hydros-TA, see "Business — Competition."

We currently have no sales organization. If we are unable to establish sales capabilities on our own, we may not be able to commercialize Hydros-TA, if approved, or commercialize any future product candidates.

We currently do not have a sales organization. In order to commercialize Hydros-TA or any future product candidates, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If one or more of our product candidates receives regulatory approval, we expect to establish a specialty sales organization with technical expertise and supporting distribution capabilities to commercialize such product candidate, which will be expensive and time consuming. As a company, we have no prior experience in the marketing, sale and distribution of pharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, comply with regulatory requirements applicable to the marketing and sale of drug products and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of Hydros-TA or any future product candidates.

We rely completely on third parties, and in some cases a single third-party, to manufacture our clinical drug supplies, and we intend to rely on third parties to produce commercial supplies of any approved product candidate. Our business would be harmed if those third parties fail to maintain approval from the FDA, fail to provide us with sufficient quantities of drug product or fail to do so at acceptable quality levels or prices.

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture our clinical drug supplies for use in the conduct of our clinical studies of Hydros-TA, and we lack the resources and the capability to manufacture Hydros-TA on a clinical or commercial scale. The facilities used by our contract manufacturers to manufacture any drug products must be approved by the FDA pursuant to inspections that will be conducted after an NDA is submitted to the FDA. We do not control the manufacturing process of Hydros-TA, and we are completely dependent on our contract manufacturing partners for compliance with the regulatory requirements, known as cGMPs, for manufacture of both active drug substances and finished drug products.

If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA withdraws approval of these facilities for the manufacture of Hydros-TA, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market Hydros-TA, if approved.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce Hydros-TA for our clinical studies. There are a limited number of suppliers for raw materials that we use to manufacture our drugs, and there may be a need to identify alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce Hydros-TA for our clinical studies, and, if approved, ultimately for commercial sale. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Although we generally do not begin a clinical study unless we believe we have on hand, or will be able to manufacture, a sufficient supply of Hydros-TA to complete such study, any significant delay or discontinuity in the supply of Hydros-TA, or the raw material components thereof, for an ongoing clinical study due to the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing and potential regulatory approval of Hydros-TA, which could harm our business and results of operations.

We may not be successful in our efforts to develop Hydros-TA for indications beyond our initial target indication of treating the pain from OA in the knee.

Hydros-TA is our only product candidate in clinical trials (currently taking place outside of the United States) with a proposed initial indication for OA pain in the knee. While our primary focus is on developing Hydros-TA for this indication, a key element of our strategy is also to expand the use of Hydros-TA into other joints in the body that are afflicted by pain associated with OA. We intend to use a portion of the proceeds from this offering to develop Hydros-TA for the treatment of OA pain in other joints in the body; however, there is no guarantee that our development efforts will be successful and the potential indications of Hydros-TA would be expanded beyond that of OA pain in the knee.

We may not be successful in our efforts to expand our pipeline of other product candidates.

Another key element of our strategy is to develop a pipeline of other product candidates. Of the large number of drugs in development, only a small percentage of such drugs successfully complete the FDA regulatory approval process and are commercialized. Accordingly, even if we are able to fund the initiation of other product development programs, we cannot assure you that any product candidates will reach the clinical-stage or be successfully developed or commercialized. Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development or commercialization for many reasons, including the following:

- the research methodology used and our drug discovery and design platform may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during our program so that the continued development of that product candidate is no longer reasonable;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable.

Even if we are successful in expanding our pipeline, through our own research and development efforts or by pursuing in-licensing or acquisition of product candidates, the potential product candidates for which we identify or acquire rights may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize a product pipeline, we may not be able to generate revenue from product sales in future periods or ever achieve profitability.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of Hydros-TA.

We face an inherent risk of product liability as a result of the clinical testing of Hydros-TA and will face an even greater risk if we commercialize Hydros-TA. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of Hydros-TA. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for Hydros-TA;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigations, product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize or co-promote Hydros-TA.

Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of any products we develop. We currently carry $5 million of product liability insurance covering use in our clinical trials in amounts that we believe are customary and adequate for a clinical-stage biopharmaceutical company. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses.

If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biopharmaceutical industry depends in large part on our ability to attract and retain highly qualified managerial, scientific and medical personnel, particularly David M. Renzi, our president and chief executive officer, Marcee M. Maroney, our vice president of clinical affairs, and David M. Gravett, Ph.D., our vice president of research and development. In order to induce valuable employees to remain with us, we have, among other things, provided stock-based compensation that vests over time. The value to employees of stock-based compensation will be significantly affected by movements in our stock price that we cannot control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and medical teams may terminate their employment with us on short notice. The loss of the services of any of our executive officers or other key employees could potentially harm our business, operating results and financial condition. Our success also depends on our ability to continue to attract, retain, and motivate highly skilled scientific and medical personnel.

We may expend our limited resources to pursue a particular product candidate or indication for Hydros-TA and fail to capitalize on product candidates or indications for Hydros-TA that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we may forego or delay pursuit of opportunities with other product candidates or for other indications of Hydros-TA that later prove to have greater commercial potential than the use of Hydros-TA for the treatment of pain associated with OA in the knee. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for future product candidates and for specific indications of Hydros-TA may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration partnerships, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance Hydros-TA through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management. Our future financial performance and our ability to commercialize Hydros-TA and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, administrative and, if necessary, sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

We may not realize the benefit of our existing collaboration partnership, may fail to form additional collaboration partnerships in the future and may not realize the benefits of such collaborations.

Our license agreement with Shanghai Jingfeng Pharmaceutical Co., Ltd., or Jingfeng, provides Jingfeng with the exclusive right and license to develop and commercialize Hydros-TA, or any improvements or modifications to Hydros-TA, for use in China, Taiwan, Hong Kong and Macau. Pursuant to the terms of the license agreement, Jingfeng is responsible for the manufacture and supply of Hydros-TA and the management

and funding of all development activities, regulatory submissions and regulatory approvals for Hydros-TA within the applicable territory. Our ability to realize any of the approximately $6.5 million in remaining milestone payments pursuant to the terms of the license agreement is therefore outside of our control and as a result we can make no guaranty or assurance that all or a portion of such payments will be made. We may form additional collaboration partnerships, create joint ventures or enter into licensing arrangements with third parties with respect to our programs that we believe will complement or augment our existing business. We have historically engaged, and intend to continue to engage, in partnering discussions with a range of pharmaceutical and biotechnology companies and could enter into new collaboration partnerships at any time. We face significant competition in seeking appropriate collaboration partners, and the negotiation process to secure appropriate terms is time-consuming and complex. Any delays in identifying suitable collaboration partners and entering into agreements to develop Hydros-TA could also delay the commercialization of Hydros-TA, which may reduce its competitiveness even if it reaches the market. Moreover, we may not be successful in our efforts to establish such a collaboration partnership for any future product candidates and programs on terms that are acceptable to us, or at all. This may be because such future product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort, our research and development pipeline may be viewed as insufficient and/or third parties may not view such product candidates and programs as having sufficient potential for commercialization, including the likelihood of an adequate safety and efficacy profile.

Even if we are successful in entering into a collaboration partnership or license arrangement, there is no guarantee that the collaboration partnership will be successful. Collaborations may pose a number of risks, including:

- collaborators often have significant discretion in determining the efforts and resources that they will apply to the collaboration, and may not commit sufficient resources to the development, marketing or commercialization of the product or products that are subject to the collaboration;
- collaborators may not perform their obligations as expected;
- any such collaboration may significantly limit our share of potential future profits from the associated program, and may require us to relinquish potentially valuable rights to product candidates, potential products or proprietary technologies or grant licenses on terms that are not favorable to us;
- collaborators may cease to devote resources to the development or commercialization of Hydros-TA or future product candidates if the collaborators view such product candidates as competitive with their own products or product candidates;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the course of development, might cause delays or termination of the development or commercialization of product candidates, and might result in legal proceedings, which would be time-consuming, distracting and expensive;
- collaborators may be impacted by changes in their strategic focus or available funding, or business combinations involving them, which could cause them to divert resources away from the collaboration;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- the collaborations may not result in us achieving revenues to justify such transactions; and
- collaborations may be terminated and, if terminated, may result in a need for us to raise additional capital to pursue further development or commercialization of the applicable product candidate.

If we seek and obtain approval to commercialize Hydros-TA outside of the United States, or otherwise engage in business outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

We may decide to seek marketing approval for Hydros-TA outside the United States or otherwise engage in business outside the United States, including entering into contractual agreements with third-parties. We expect that we will be subject to additional risks related to entering into these international business markets and relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- differing United States and foreign drug import and export rules;
- reduced protection for intellectual property rights in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems, and different competitive drugs;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- potential liability resulting from development work conducted by these distributors; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

Our business involves the use of hazardous materials and we and third-parties with whom we contract must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our research and development activities involve the controlled storage, use and disposal of hazardous materials, including the components of Hydros-TA and other hazardous compounds. We and manufacturers and suppliers with whom we may contract are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly

clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. We cannot guarantee that that the safety procedures utilized by third-party manufacturers and suppliers with whom we may contract will comply with the standards prescribed by laws and regulations or will eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. We do not currently carry biological or hazardous waste insurance coverage.

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data from completed or ongoing clinical trials for Hydros-TA could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of Hydros-TA or future product candidates could be delayed.

We may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters and other facilities are located in the San Francisco Bay Area, which in the past has experienced severe earthquakes. We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

The terms of our loan and security agreement may restrict our ability to engage in certain transactions.

In October 2011, we entered into a loan and security agreement with Silicon Valley Bank, or SVB. Pursuant to the terms of the loan and security agreement subject to certain exceptions, we cannot engage in certain transactions, unless certain conditions are met or we receive the prior approval of SVB. Such transactions include:

- disposing of our business or certain assets;
- changing our business, management, ownership or business locations;

- incurring additional debt or liens or making payments on other debt;
- making certain investments and declaring dividends;
- acquiring or merging with another entity;
- engaging in transactions with affiliates; or
- encumbering intellectual property.

If SVB does not provide its consent to such actions we could be prohibited from engaging in transactions that could be beneficial to our business and our stockholders unless we were to repay the loans, which may not be desirable or possible. The loan and security agreement is collateralized by a pledge of substantially all of our assets, except for intellectual property. If we were to default under the loan and security agreement, including for an inability to repay amounts as they become due, and were unable to obtain a waiver for such a default, SVB would have a right to accelerate our obligation to repay the entire loan and foreclose on these assets in order to satisfy our obligations under the loan and security agreement. In addition, SVB would also have the right to place a hold on our accounts maintained at SVB and refuse to fund any then unfunded commitments under the loan and security agreement. Any such action on the part of SVB against us could have a materially adverse impact on our business, financial condition and results of operations.

Risks Related to Government Regulation

The regulatory approval processes of the FDA are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for Hydros-TA, our business will be substantially harmed.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States. We are not permitted to market any drug product in the United States until we receive marketing approval from the FDA. We have not submitted an application or obtained marketing approval for Hydros-TA anywhere in the world. Obtaining regulatory approval of a new drug application, or NDA, can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable United States regulatory requirements may subject us to administrative or judicially imposed sanctions or other actions, including:

- warning letters;
- civil and criminal penalties;
- injunctions;
- withdrawal of regulatory approval of products;
- product seizure or detention;
- product recalls;
- total or partial suspension of production; and
- refusal to approve pending NDAs or supplements to approved NDAs.

Prior to obtaining approval to commercialize a drug candidate in the United States or abroad, we or our collaboration partners must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA, that such drug candidates are safe and effective for their intended uses. We are actively enrolling patients internationally in COR1.1, which is our first Phase 3 clinical trial of Hydros-TA, and we expect to initiate COR1.2, our second Phase 3 clinical trial of Hydros-TA, in mid-2015. We expect to report primary endpoint results from COR1.1 in early 2016 and from COR1.2 by the end of 2016, and to submit our NDA for Hydros-TA in early 2017. The number of nonclinical studies and clinical trials that will be required for FDA approval varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate and, as such, we may be required to perform additional clinical trials beyond our ongoing COR1.1 trial and our expected COR1.2 trial. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our drug candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering drug candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials and result in the FDA or other regulatory authorities denying approval of a drug candidate for any or all targeted indications.

Regulatory approval of an NDA is not guaranteed and the time required to obtain approval is unpredictable, typically takes many years following the commencement of clinical studies, and depends upon numerous factors. The FDA has substantial discretion in the approval process and we may encounter matters with the FDA that require us to expend additional time and resources and which may delay or prevent the approval of Hydros-TA. For example, the FDA may require us to conduct additional studies or trials for Hydros-TA either prior to or post-approval, such as additional drug-drug interaction studies or safety or efficacy studies or trials, or it may object to elements of our clinical development program such as the number of subjects in our current clinical trials from the United States. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of Hydros-TA's clinical development, which may cause delays in the approval or result in a decision not to approve an application for regulatory approval. Despite the time and expense exerted, failure can occur at any stage. An NDA for Hydros-TA could fail to receive FDA approval for many reasons, including but not limited to the following:

- the FDA may disagree with the design or implementation of our clinical studies;
- the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which approval is sought;
- the FDA may disagree with the interpretation of data from pre-clinical studies or clinical studies;
- the data collected from clinical studies of Hydros-TA may not be sufficient to support the submission of a NDA or to obtain FDA approval;
- we may be unable to demonstrate to the FDA that Hydros-TA's risk-benefit ratio for its proposed indication is acceptable;
- the FDA may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers responsible for clinical and commercial supplies; and
- the approval policies or regulations of the FDA may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical studies, may result in our failure and/or that of a collaboration partner to obtain regulatory approval to market Hydros-TA, which would significantly harm our business, results of operations, and prospects. Additionally, if the FDA requires that we conduct additional clinical studies or delays or refuses approval to market Hydros-TA, our business and results of operations may be harmed.

In addition, even if we were to obtain approval, the FDA may approve Hydros-TA for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve Hydros-TA with a label that does not include the labeling claims necessary or desirable for successful commercialization. Any of the foregoing scenarios could materially harm the commercial prospects for Hydros-TA.

Third-party payor coverage and reimbursement status of newly-approved products is uncertain and such coverage for viscosupplementation may be hampered by recommendations from AAOS. Failure to obtain or maintain adequate coverage and reimbursement for Hydros-TA, if approved, could limit our ability to market Hydros-TA and decrease our ability to generate revenue.

The pricing, coverage and reimbursement of Hydros-TA, if approved, must be adequate to support a commercial infrastructure. The availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to be able to afford treatments such as ours, assuming approval. Sales of Hydros-TA will depend substantially, on the extent to which the costs of Hydros-TA will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other third-party payors. If coverage and reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize Hydros-TA. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered and reimbursed. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies established. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

In addition to the risks faced by all newly-approved products, we face additional risks as a result of the current clinical practice guidelines issued by AAOS relating to viscosupplementation in OA of the knee. AAOS's current clinical practice guidelines, which many payors rely upon when developing their coverage policies relating to viscosupplementation, do not recommend intra-articular use of HA in patients with symptomatic OA of the knee. While some third-party payors continue to cover HA for the treatment of OA of the knee after the publication of these guidelines, a number of third-party payors, including Blue Cross Blue Shield, have reversed their coverage policies and no longer cover the use of HA for the treatment of OA of the knee. If AAOS does not revise these guidelines to reflect a more positive recommendation with respect to viscosupplementation or Hydros-TA, and/or other organizations (including, but not limited to, governmental agencies, other professional societies, private health and science foundations and practice management groups) release similar guidelines suggesting reduced use of HA or promote competitive or alternative therapies, additional payors may reverse currently positive coverage policies or refuse to approve Hydros-TA for coverage and reimbursement which could limit our ability to market Hydros-TA and decrease our ability to generate revenue.

Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Reimbursement rates may vary depending on the payor, the insurance plan, and other factors. A current trend in the United States health care industry is toward cost containment. Large public and private payors, managed care organizations, group purchasing organizations and similar organizations are exerting increasing influence on decisions regarding the use of, and reimbursement levels of, particular treatments. Such third-party payors, including Medicare, are questioning the coverage of, and challenging the prices charged for medical products and services. Moreover, increasing efforts by governmental and third-party payors in the United States to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products approved and, as a result, these caps may not cover or provide adequate payment for Hydros-TA. We expect to experience pricing pressures in connection with the sale of Hydros-TA due to the trend toward managed healthcare,

the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Adequate third-party coverage and reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development, which could adversely impact our revenue and prospects for profitability. We cannot provide any assurances that we will be able to obtain and maintain third-party coverage or adequate reimbursement for our drug candidates in whole or in part.

If the FDA does not conclude that Hydros-TA satisfies the requirements for the 505(b)(2) regulatory approval pathway, or if the requirements for approval of Hydros-TA under Section 505(b)(2) are not as we expect, the approval pathway for Hydros-TA will likely take significantly longer, cost significantly more and encounter significantly greater complications and risks than anticipated, and in any case may not be successful.

We intend to seek FDA approval through the 505(b)(2) regulatory pathway for Hydros-TA. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, added Section 505(b)(2) to the Federal Food, Drug and Cosmetic Act, or FDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference. If the FDA does not allow us to pursue the 505(b)(2) regulatory pathway for Hydros-TA as anticipated, we may need to conduct additional clinical trials, provide additional data and information and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for Hydros-TA would likely substantially increase. Moreover, the inability to pursue the 505(b)(2) regulatory pathway could result in new competitive products reaching the market faster than Hydros-TA, which could materially adversely impact our competitive position and prospects. Even if we are allowed to pursue the 505(b)(2) regulatory pathway for Hydros-TA, we cannot assure you that we will receive the requisite or timely approvals for commercialization.

Even if we receive regulatory approval for Hydros-TA, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, if approved, Hydros-TA could be subject to labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Even if a drug is approved by the FDA, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with GCPs for any clinical trials that we conduct post-approval. In addition, manufacturers and manufacturers' facilities are require to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs. As such, we and our third-party contract manufacturers will be subject to continual review and periodic inspections to assess compliance with regulatory requirements. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. Regulatory authorities may also impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-marketing studies. Furthermore, any new legislation addressing drug safety issues could result in delays or increased costs to assure compliance.

We will also be required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have FDA approval.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- warning letters or fines;
- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market or voluntary or mandatory product recalls;
- injunctions or the imposition of civil or criminal penalties;
- suspension or revocation of existing regulatory approvals;
- suspension of any of our ongoing clinical trials;
- refusal to approve pending applications or supplements to approved applications submitted by us;
- restrictions on our or our contract manufacturers' operations; or
- product seizure or detention, or refusal to permit the import or export of products.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize Hydros-TA. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

In addition, the FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of Hydros-TA. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We and our contract manufacturers are subject to significant regulation with respect to manufacturing Hydros-TA. The manufacturing facilities on which we rely may not continue to meet regulatory requirements or may not be able to meet supply demands.

All entities involved in the preparation of product candidates for clinical studies or commercial sale, including our existing contract manufacturers for Hydros-TA, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. We or our contract manufacturers must supply all necessary documentation in support of an NDA on a timely basis and must adhere to cGMP regulations enforced by the FDA. Some of our contract manufacturers have never produced a commercially approved pharmaceutical product and therefore have not obtained the requisite regulatory authority approvals to do so. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of Hydros-TA. In addition, the FDA may, at any time, inspect a manufacturing facility involved with the preparation of Hydros-TA or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If our contract manufacturers cannot successfully manufacture material that conforms

to our specifications and the strict regulatory requirements of the FDA, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the product candidates manufactured at these facilities may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel.

The regulatory authorities also may, at any time following approval of a product for sale, inspect the manufacturing facilities of our third-party contractors. If any such inspection identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third-party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent suspension of production or closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If a third-party manufacturer with whom we contract fails to maintain regulatory compliance, the FDA may impose regulatory sanctions including, among other things, refusal to approve Hydros-TA or withdrawal of approval for Hydros-TA if previously approved. In addition, we may be subject to fines, unanticipated compliance expenses, recall or seizure, total or partial suspension of production and/or enforcement actions, including injunctions and criminal or civil prosecution. These possible sanctions would adversely affect our financial results and financial condition.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through a supplemental NDA, which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause us to incur higher costs and could cause the delay or termination of clinical studies, regulatory submissions, required approvals, or commercialization of Hydros-TA. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenue.

If approved, Hydros-TA may cause or contribute to adverse medical events that we are required to report to regulatory agencies, and if we fail to do so, we could be subject to sanctions that could materially harm our business.

Some participants in clinical studies of Hydros-TA have reported adverse effects after being treated with Hydros-TA, including injection site pain, arthralgia, meniscal lesion and cyst aspiration. If we are successful in commercializing Hydros-TA, FDA regulations require that we report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we fail to comply with our reporting obligations, the FDA could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products.

If we fail to comply or are found to have failed to comply with FDA and other regulations related to the promotion of Hydros-TA for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other government agencies. If we receive marketing approval for Hydros-TA, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. We intend to implement compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of Hydros-TA for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses. Over the past several years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various federal and state laws and regulations, including claims asserting antitrust violations, violations of the Food, Drug and Cosmetic Act, the False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. Many of these investigations originate as "qui tam" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim, or caused a false claim to be submitted, to the government for payment. The person bringing a qui tam suit is entitled to a share of any recovery or settlement. Qui tam suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a qui tam suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

We are currently only seeking regulatory approval to market Hydros-TA in the United States, and if we want to expand the geographies in which we may market Hydros-TA, we will need to obtain additional regulatory approvals. Our failure to obtain regulatory approvals in foreign jurisdictions for Hydros-TA would prevent us from marketing internationally.

We currently plan to seek regulatory approval for Hydros-TA in the United States. In the future, we may attempt to seek regulatory approval to promote and commercialize Hydros-TA outside of the United States. In order to obtain such approvals, we may be required to conduct additional clinical trials or studies to support our applications, which would be time consuming and expensive, and may produce results that do not result in regulatory approvals. Further, we will have to expend substantial time and resources in order to establish the commercial infrastructure necessary to promote and commercialize Hydros-TA outside of the United States, or pursue a collaboration arrangement that would enable such promotion and commercialization. If we do not obtain regulatory approvals for Hydros-TA in foreign jurisdictions, our ability to expand our business outside the United States will be severely limited.

The approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the FDA does not

ensure approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not be able to file for regulatory approvals or to do so on a timely basis, and even if we do file we may not receive necessary approvals to commercialize our products in any market.

Healthcare legislative reforms in the United States may make it more difficult and costly for us to obtain regulatory clearance or approval of Hydros-TA and to produce, market and distribute Hydros-TA after clearance or approval is obtained.

In the United States, there have been and continue to be a number of legislative initiatives that could significantly change the statutory provisions governing the regulatory clearance or approval, manufacture, and marketing of regulated products or the coverage and reimbursement thereof. In addition, FDA regulations and guidance are often revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of Hydros-TA. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;
- changes to manufacturing methods;
- recall, replacement, or discontinuance of one or more of our products; and
- additional record keeping.

Each of these would likely entail substantial time and cost and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any future products would harm our business, financial condition and results of operations.

In addition, the full impact of recent healthcare reform and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model. In the United States, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act was enacted in 2010 with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers.

Further, third-party payors regularly update payments to physicians and hospitals where our product candidates will be used. Because viscosupplement injection is performed by the physician, usually in the office or outpatient clinic, payors generally reimburse the physician for both the IA injection and for the viscosupplement. As a result, these payment updates could directly impact the demand for our product candidates, if approved.

It is likely that federal and state legislatures within the United States will continue to consider changes to existing healthcare legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect the demand for any drug products for which we may obtain regulatory approval, our ability to set a price that we believe is fair for our products, our ability to obtain coverage and reimbursement approval for a product, our ability to generate revenues and achieve or maintain profitability, and the level of taxes that we are required to pay.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain FDA approval for Hydros-TA or any future product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations. These laws may impact, among other things, our proposed sales, marketing, and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology and Clinical Health Act and its implementing regulations, which imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information;

- the federal physician sunshine requirements under the Affordable Care Act require manufacturers of drugs, devices, biologics, and medical supplies to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers, state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the Affordable Care Act, among other things, amends the intent requirement of the federal Anti-Kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Related to Intellectual Property

We may become subject to claims alleging infringement of third parties' patents or proprietary rights and/or claims seeking to invalidate our patents, which would be costly, time consuming and, if successfully asserted against us, delay or prevent the development and commercialization of Hydros-TA or any future product candidates.

Our commercial success depends in part on avoiding infringement and misappropriation of the patents and proprietary rights of third parties. There have been many lawsuits and other proceedings asserting infringement or misappropriation of patents and other intellectual property rights in the pharmaceutical and biotechnology industries, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the U.S. Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. As the pharmaceutical and biotechnology industries expand and more patents are issued in this area, the risk increases that Hydros-TA and any future product candidates may be subject to claims of infringement of the patent rights of third parties.

We cannot assure you that we will not be subject to claims alleging that the manufacture, use or sale of Hydros-TA or any future product candidates nor that any activities conducted by us, infringes existing or future third-party patents, or that such claims, if any, will not be successful. We cannot guarantee that we have identified each and every patent and pending application in the United States and abroad owned by others that is relevant or necessary to the commercialization of Hydros-TA. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of Hydros-TA or future product candidates or by the operation of our business. We may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of Hydros-TA or future product candidates. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect.

In addition, coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that Hydros-TA or future product candidates either do not infringe the patent claims of the relevant patent or that the patent claims are invalid and/or unenforceable, and we may not be able to do this. Proving that a patent is invalid or unenforceable is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Also in proceedings before the courts in Europe, the burden of proving invalidity of the patent usually rests on the party alleging invalidity. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

We may be subject to third-party patent infringement claims in the future against us or a collaboration partner that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing a third-party's patents. We may be required to indemnify our collaboration partners against such claims. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be

necessary to defend against such claims. If a patent infringement suit were brought against us or our collaboration partners, we or they could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. As a result of patent infringement claims, or in order to avoid potential claims, we or our collaboration partners may choose to seek, or be required to seek, a license from the third-party and would most likely be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we or our collaboration partners were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or forced to redesign it, or to cease some aspect of our business operations if, as a result of actual or threatened patent infringement claims, we or our collaboration partners are unable to enter into licenses on acceptable terms. Even if we are successful in defending against such claims, such litigation can be expensive and time consuming to litigate and would divert management's attention from our core business. Any of these events could harm our business significantly.

In addition to infringement claims against us, if third parties prepare and file patent applications in the United States that also claim technology similar or identical to ours, we may have to participate in interference or derivation proceedings in the United States Patent and Trademark Office, or the USPTO, to determine which party is entitled to a patent on the disputed invention. We may also become involved in similar opposition proceedings in the European Patent Office or similar offices in other jurisdictions regarding our intellectual property rights with respect to our products and technology. Since patent applications are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to Hydros-TA or any future product candidates. An unfavorable outcome in any such proceedings could require us to cease using the related technology or to attempt to license rights to it from the prevailing party or could cause us to lose valuable intellectual property rights. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms, if any license is offered at all. Even if we are successful in these proceedings, these proceedings may result in substantial costs and distract our management and other employees.

If our intellectual property related to Hydros-TA is not adequate or if we are not able to protect our trade secrets or our confidential information, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to Hydros-TA, our drug discovery and development platform and our development programs. Any disclosure to or misappropriation by third parties of our confidential or proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or license may fail to result in issued patents in the United States or in foreign countries. Even if patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. For example, U.S. patents can be challenged by any person before the new USPTO Patent Trial and Appeals Board at any time before one year after that person is served an infringement complaint based on the patents. Patents granted by the European Patent Office may be similarly opposed by any person within nine months from the publication of the grant. Similar proceedings are available in other jurisdictions, and in the United States, Europe and other jurisdictions third parties can raise questions of validity with a patent office even before a patent has granted. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. For example, a third-party may develop a competitive product that provides therapeutic benefits similar to Hydros-TA but has a sufficiently different composition to fall outside the scope of our patent protection. If the breadth or strength of protection provided by the patents and patent applications we hold or pursue with respect to Hydros-TA is

successfully challenged, then our market for Hydros-TA could be negatively affected, and we may face unexpected competition that could have a material adverse impact on our business. Further, if we encounter delays in our clinical trials, the period of time during which we could market Hydros-TA under patent protection would be reduced.

Even where laws provide protection, costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and the outcome of such litigation would be uncertain. If we or a collaboration partner were to initiate legal proceedings against a third-party to enforce a patent covering Hydros-TA, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability against our intellectual property related to Hydros-TA, we would lose at least part, and perhaps all, of the patent protection on Hydros-TA. Such a loss of patent protection would have a material adverse impact on our business. Moreover, our competitors could counterclaim that we infringe their intellectual property, and some of our competitors have substantially greater intellectual property portfolios than we do.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of the hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We also rely on trade secret protection and confidentiality agreements to protect proprietary know-how that may not be patentable, processes for which patents may be difficult to obtain and/or enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology, to assign their inventions to us, and endeavor to execute confidentiality agreements with all such parties, we cannot be certain that we have executed such agreements with all parties who may have helped to develop our intellectual property or who had access to our proprietary information, nor can we be certain that our agreements will not be breached by such consultants, advisors or third parties, or by our former employees. The breach of such agreements by individuals or entities who are actively involved in the discovery and design of our potential drug candidates, could require us to pursue legal action to protect our trade secrets and confidential information, which would be expensive, and the outcome of which would be unpredictable. If we are not successful in prohibiting the continued breach of such agreements, our business could be negatively impacted. We cannot guarantee that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

An NDA submitted under Section 505(b)(2) subjects us to the risk that we may be subject to a patent infringement lawsuit that would delay or prevent the review or approval of Hydros-TA.

We intend to rely on Section 505(b)(2) for our NDA submission of Hydros-TA. A 505(b)(2) application for Hydros-TA would enable us to reference published literature and/or the FDA's previous findings of safety and effectiveness for the branded reference drug. For NDAs submitted under Section 505(b)(2) of the FDCA, the patent certification and related provisions of the Hatch-Waxman Act apply. In accordance with the Hatch-Waxman Act, such NDAs may be required to include certifications, known as paragraph IV certifications, that certify that any patents listed in the FDA's publication, Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book, with respect to any product referenced in the 505(b)(2) application, are invalid, unenforceable or will not be infringed by the manufacture, use or sale of the product that is the subject of the 505(b)(2) NDA. If a 505(b)(2) applicant makes a paragraph IV certification, it must give notice of that certification to the owner of the patent and the holder of the approved NDA for the reference drug.

Under the Hatch-Waxman Act, the holder of patents that the 505(b)(2) application references may file a patent infringement lawsuit after receiving notice of the paragraph IV certification. Filing of a patent infringement lawsuit against the filer of the 505(b)(2) applicant within 45 days of the patent owner's receipt of notice triggers a one-time, automatic, 30-month stay of the FDA's ability to approve the 505(b)(2) NDA, unless patent litigation is resolved in the favor of the paragraph IV filer or the patent expires before that time. In addition, a 505(b)(2) application will not be approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, or NCE, listed in the Orange Book for the referenced product has expired. The FDA may also require us to perform one or more additional clinical studies or measurements to support the change from the branded reference drug, which could be time consuming and could substantially delay our achievement of regulatory approval for Hydros-TA. The FDA may also reject our 505(b)(2) submission and require us to file such submission under Section 505(b)(1) of the FDCA, which would require us to provide extensive data to establish safety and effectiveness of the drug for the proposed use and could cause delay and be considerably more expensive and time consuming. These factors, among others, may limit our ability to successfully commercialize Hydros-TA.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation, including the Leahy-Smith America Invents Act signed into law on September 16, 2011. That Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and new venues and opportunities for competitors to challenge patent portfolios. Because of that Act, the U.S. patent system is now a "first to file" system, which may make it more difficult to obtain patent protection for inventions and increase the uncertainties and costs surrounding the prosecution of our or a collaboration partners' patent applications and the enforcement or defense of our or a collaboration partners' issued patents, all of which could materially adversely affect our business, results of operations and financial condition.

The United States Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions to maintain patent applications and issued patents. Noncompliance with these requirements can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

We may not be able to enforce our intellectual property rights throughout the world.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain and enforce adequate intellectual property protection for our technology.

We may be subject to claims that we or our employees have misappropriated the intellectual property, including know-how or trade secrets, of a third-party, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, consultants and contractors were previously employed at or engaged by other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, consultants and contractors, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees, consultants and contractors do not use the intellectual property and other proprietary information or know-how or trade secrets of others in their work for us, and do not perform work for us that is in conflict with their obligations to another employer or any other entity, we may be subject to claims that we or these employees, consultants and contractors have used or disclosed such intellectual property, including know-how, trade secrets or other proprietary information. In addition, an employee, advisor or consultant who performs work for us may have obligations to a third-party that are in conflict with their obligations to us, and as a result such third-party may claim an ownership interest in the intellectual property arising out of work performed for us. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, or access to consultants and contractors. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that

we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

Risks Related to Our Common Stock, This Offering and being a Public Company

Our stock price may be volatile and you may not be able to resell shares of our common stock at or above the price you paid.

The trading price of our common stock following this offering could be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include those discussed in this "Risk Factors" section of this prospectus and others such as:

- results from, or any delays in, clinical trial programs relating to Hydros-TA, including slower than anticipated enrollment;
- ability to commercialize or obtain regulatory approval for Hydros-TA, or delays in commercializing or obtaining regulatory approval;
- announcements of regulatory approval or a complete response letter to Hydros-TA, or specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- changes in reimbursement or third-party coverage of treatments for pain associated with OA, or changes to treatment recommendations or guidelines applicable to the treatment of OA or pain from OA;
- announcements relating to collaboration partnerships or other strategic transactions undertaken by us;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to Hydros-TA;
- any adverse changes to our relationship with any manufacturers or suppliers;
- the success of our testing and clinical trials;
- the success of our efforts to acquire or license or discover additional product candidates;
- any intellectual property infringement actions in which we may become involved;
- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our operating results;

- FDA or other U.S. regulatory actions affecting us or our industry or other healthcare reform measures in the United States;
- changes in financial estimates or recommendations by securities analysts;
- trading volume of our common stock;
- sales of our common stock by us, our executive officers and directors or our stockholders in the future;
- general economic and market conditions and overall fluctuations in the United States equity markets; and
- the loss of any of our key scientific or management personnel.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business, which could seriously harm our financial position. Any adverse determination in litigation could also subject us to significant liabilities.

We have broad discretion to determine how to use the funds raised in this offering, and may use them in ways that may not enhance our operating results or the price of our common stock.

We currently intend to use substantially all of the net proceeds of this offering to fund our COR1.1 and COR1.2 trials, and the balance for working capital and other corporate purposes, which may include the pursuit of other research and discovery efforts, including the development of Hydros-TA for the treatment of OA pain in other joints in the body. However, within the scope of our plan, and in light of the various risks to our business that are set forth in this section, our management will have broad discretion over the use of proceeds from this offering, and we could spend the proceeds from this offering in ways our stockholders may not agree with or that do not yield a favorable return, if at all. If we do not invest or apply the proceeds of this offering in ways that improve our operating results, we may fail to achieve expected financial results, which could cause our stock price to decline.

An active, liquid and orderly market for our common stock may not develop, and you may not be able to resell your common stock at or above the public offering price.

Prior to this offering, there has been no public market for shares of our common stock, and an active public market for our shares may not develop or be sustained after this offering. We and Leerink Partners, as representative of the underwriters, have determined the initial public offering price of our common stock through negotiation. This price will not necessarily reflect the price at which investors in the market will be willing to buy and sell our shares following this offering. In addition, an active trading market may not develop following the closing of this offering or, if it is developed, may not be sustained. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. An inactive market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses or technologies or in-license new product candidates using our shares as consideration.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not currently have and may never obtain research

coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, the trading price for our stock would be negatively impacted. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

We will incur significant costs as a result of operating as a public company, and our management will devote substantial time to new compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes-Oxley Act of 2002, which could result in sanctions or other penalties that would harm our business.

We will incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and regulations regarding corporate governance practices. The listing requirements of The NASDAQ Global Market require that we satisfy certain corporate governance requirements relating to director independence, distributing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel will need to devote a substantial amount of time to ensure that we comply with all of these requirements, and we will likely need to hire additional accounting and financial staff with appropriate public company reporting experience and technical accounting knowledge. Moreover, the reporting requirements, rules and regulations will increase our legal and financial compliance costs and will make some activities more time consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms.

After this offering, we will be subject to Section 404 of The Sarbanes-Oxley Act of 2002, or Section 404, and the related rules of the Securities and Exchange Commission, or SEC, which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Beginning with the second annual report that we will be required to file with the SEC, Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting. However, for so long as we remain an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404. See below, "We are eligible to be treated as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors" for a further discussion of the impacts of our decision to take advantage of the exceptions available to emerging growth companies.

To date, we have never conducted a review of our internal control for the purpose of providing the reports required by these rules. During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal control over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the

trading price of our stock to fall. In addition, as a public company we will be required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The NASDAQ Global Market or other adverse consequences that would materially harm our business.

If we fail to maintain proper internal controls, our ability to produce accurate financial statements or comply with applicable regulations could be impaired.

Pursuant to Section 404 of the Sarbanes-Oxley Act, our management is required annually to deliver a report that assesses the effectiveness of our internal control over financial reporting and, subject to exemptions allowed as an "emerging growth company," our independent registered public accounting firm is required annually to deliver an attestation report on the effectiveness of our internal control over financial reporting. If we are unable to maintain effective internal control over financial reporting or if our independent registered public accounting firm is unwilling or unable to provide us with an attestation report on the effectiveness of internal control over financial reporting for future periods as required by Section 404 of the Sarbanes-Oxley Act, we may not be able to produce accurate financial statements, and investors may therefore lose confidence in our operating results, our stock price could decline and we may be subject to litigation or regulatory enforcement actions.

We are eligible to be treated as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board providing for supplemental auditor's reports for additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting burdens in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive by relying on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have total annual gross revenue of $1.0 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, we would cease to be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" if the market value of our common stock held by non-affiliates is below $75.0 million as of June 30 in any given year, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

Purchasers in this offering will experience immediate and substantial dilution in the book value of their investment.

The initial public offering price of our common stock is substantially higher than the pro forma net tangible book value per share of our common stock before giving effect to this offering. Accordingly, if you purchase our common stock in this offering, you will incur immediate substantial dilution of approximately $2.47 per share, based on the initial public offering price of $5.00 per share and our pro forma net tangible book value as of December 31, 2014. In addition, following this offering, purchasers in this offering will have contributed approximately 46% of the total gross consideration paid by stockholders to us to purchase shares of our common stock, but will own only approximately 54% of the shares of common stock outstanding immediately after this offering. Furthermore, if the underwriters exercise their option to purchase additional shares, or outstanding options or convertible securities are exercised, you could experience further dilution. For a further description of the dilution that you will experience immediately after this offering, see the section titled "Dilution."

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights, including rights to Hydros-TA, our technologies or future product candidates, on unfavorable terms to us.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings and license and development agreements through strategic partnerships with third parties. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic partnerships with third parties, we may have to relinquish valuable rights to Hydros-TA, our technologies, future revenue streams, research programs or future product candidates or grant licenses on terms that are not favorable to us. If we are unable to raise additional capital when needed, we would be required to delay, limit, reduce or terminate our product development or commercialization efforts for Hydros-TA, or grant rights to develop and market future product candidates that we would otherwise prefer to develop and market ourselves.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the trading price of our common stock could decline. Based upon the number of shares outstanding as of December 31, 2014, upon the closing of this offering, we will have outstanding a total of 24,246,963 shares of common stock,

assuming no exercise of the underwriters' option to purchase additional shares. Of these shares, approximately 13,000,000 shares of our common stock, plus any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable, without restriction, in the public market immediately following this offering. Leerink Partners LLC, however, may, in their sole discretion, permit our officers, directors and other stockholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus. After the lock-up agreements expire, as of March 1, 2015, and including the conversion of our convertible promissory notes and accrued interest thereon into 2,287,120 shares of common stock immediately prior to the closing of this offering, up to an additional 11,264,107 shares of common stock will be eligible for sale in the public market, 10,955,516 of which shares are beneficially owned by current directors, executive officers and other affiliates and may be subject to Rule 144 under the Securities Act of 1933, or the Securities Act. The underwriters may, however, in their sole discretion, permit our officers, directors and other stockholders and the holders of our outstanding options who are subject to the lock-up agreements to sell shares prior to the expiration of the lock-up agreements. Sales of these shares, or perceptions that they will be sold, could cause the trading price of our common stock to decline.

In addition, as of December 31, 2014, 1,328,873 shares of common stock that are subject to outstanding options with a weighted average exercise price of $2.54 per share will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

After this offering, the holders of approximately 8,268,531 shares of our outstanding common stock as of December 31, 2014 will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to vesting schedules and to the lock-up agreements described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of March 1, 2015, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 91.6% of our outstanding voting stock and, upon the closing of this offering, that same group will hold approximately 56.4% of our outstanding voting stock (assuming no exercise of the underwriters' option to purchase additional shares and no exercise of outstanding options). Therefore, even after this offering these stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws that will be in effect immediately prior to the closing of this offering will contain provisions that could significantly reduce the value of our shares to a potential acquirer or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents will include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the required approval of at least 66 $^{2}/_{3}$% of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of at least 66 $^{2}/_{3}$% of the shares entitled to vote at an election of directors to adopt, amend or repeal certain provisions of our bylaws and our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by or at the direction of our board of directors pursuant to a resolution adopted by a majority of the total number of directors that our board of directors would have if there were no vacancies, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

In addition, these provisions would apply even if we were to receive an offer that some stockholders may consider beneficial.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction. For a description of our capital stock, see "Description of Capital Stock."

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws to be effective immediately prior to the completion of this offering and our indemnification agreements that we have entered into with our directors and officers provide that:

- We will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.

- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.

- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.

- We will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.

- The rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.

- We may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

Our ability to use our net operating losses to offset future taxable income, if any, may be subject to certain limitations.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" (generally defined as a greater than 50-percentage-point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three-year period) is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, to offset future taxable income. We experienced an ownership change in December 2005 that limited our use of approximately $0.3 million of the approximately $44.2 million of NOLs available to us for federal income tax purposes as of December 31, 2014. If we undergo additional ownership changes in connection with or after this offering (some of which changes may be outside our control), our ability to utilize our NOLs could be further limited by Section 382 of the Code. Our NOLs may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs. Furthermore, our ability to utilize our NOLs is conditioned upon our attaining profitability and generating U.S. federal taxable income. We have incurred net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; thus, we do not know whether or when we will generate the U.S. federal taxable income necessary to utilize our NOLs. See the risk factors described above under "—Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements."

We do not currently intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. In addition, pursuant to our loan and security agreement with SVB, we are prohibited from paying cash dividends without the prior consent of SVB. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

Special Note Regarding Forward-Looking Statements

This prospectus contains forward-looking statements. The forward-looking statements are contained principally in the sections entitled “Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business.” These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the success, cost and timing of our product development activities and clinical trials and projections as to the timing of clinical studies and regulatory submissions;
- our ability to obtain and maintain regulatory approval of Hydros-TA, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations beyond this offering, including funding necessary to complete clinical development and file an IND and NDA for Hydros-TA;
- our plans to develop and successfully commercialize Hydros-TA and other product candidates;
- the size and growth potential of the markets for Hydros-TA, and our ability to serve those markets;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- the rate and degree of market acceptance of Hydros-TA;
- regulatory developments in the United States and foreign countries;
- the potential, and our ability, to successfully expand the potential indications for Hydros-TA beyond treatment of pain in the knee caused by OA;
- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or become available;
- the loss of key scientific or management personnel;
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act;
- our use of the proceeds from this offering and the sufficiency of our capital resources;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and
- our expectations regarding our ability to obtain and adequately maintain sufficient intellectual property protection for our current or future product candidates.

In some cases, you can identify these statements by terms such as “anticipate,” “believe,” “could,” “estimate,” “expects,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” or the negative of those terms, and similar expressions. These forward-looking statements reflect our management’s

beliefs and views with respect to future events and are based on estimates and assumptions as of the date of this prospectus and are subject to risks and uncertainties. We discuss many of these risks in greater detail under the heading “Risk Factors.” Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in this prospectus by these cautionary statements. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this prospectus. See “Where You Can Find Additional Information.”

These forward-looking statements speak only as of the date of this prospectus. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

Use of Proceeds

The net proceeds from the sale of the shares of our common stock in this offering will be approximately $57.1 million, or $66.1 million if the underwriters fully exercise their option to purchase additional shares, based upon the initial public offering price of $5.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We currently estimate that we will use the net proceeds that we will receive from this offering as follows:

- approximately $25.0 million to $35.0 million to fund our continued research and discovery efforts, including to fund to completion both our ongoing COR1.1 and our future COR1.2 Phase 3 clinical trials of Hydros-TA in support of an NDA filing with the FDA;
- the remainder for working capital and other corporate purposes, which may include the pursuit of other research and discovery efforts, including the development of Hydros-TA for the treatment of OA pain in other joints in the body.

We may also use a portion of the net proceeds from this offering to repay our secured debt facility with Silicon Valley Bank, under which we owe approximately $5.0 million in principal and interest as of December 31, 2014. For additional information related to our outstanding loan, including the interest rate and maturity, see “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations—Indebtedness.” We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses, technologies, products or assets. However we have no current plan, commitments or obligations to do so.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from nonclinical testing or clinical trials, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

We believe that the net proceeds from this offering and our existing cash and cash equivalents will allow us to fund our operating plan through at least the next 12 months.

Pending the use of the proceeds from this offering, we intend to invest the net proceeds in interest-bearing, investment-grade securities, certificates of deposit or government securities.

Dividend Policy

We have never declared or paid any cash dividends on our common stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. In addition, pursuant to our loan and security agreement with Silicon Valley Bank, we are prohibited from paying cash dividends without the prior consent of Silicon Valley Bank. Any future determination related to our dividend policy will be made at the discretion of our board of directors.

Capitalization

The following table sets forth our cash and cash equivalents, and our total capitalization as of December 31, 2014:

- on an actual basis;
- on a pro forma basis, giving effect to (i) the automatic conversion of all our outstanding shares of convertible preferred stock into an aggregate of 8,268,531 shares of our common stock, (ii) the related reclassification of the preferred stock warrant liability to additional paid-in-capital and (iii) the conversion of our September 2014 and February 2015 convertible promissory notes and 184 days and 41 days, respectively, of accrued interest thereon into 2,287,120 shares of common stock and the resulting loss on extinguishment of $3.6 million based on the initial public offering price of $5.00 per share, in each case, immediately prior to the closing of this offering; and
- on a pro forma as adjusted basis, giving further effect to the sale by us of 13,000,000 shares of our common stock in this offering at the initial public offering price of $5.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma and pro forma as adjusted information below is illustrative only, and our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table together with our financial statements and the related notes appearing at the end of this prospectus, the sections entitled “Selected Financial Data” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and other financial information appearing elsewhere in this prospectus.

	As of December 31, 2014		
	Actual	Pro Forma	Pro Forma As Adjusted
	(in thousands, except share and per share amounts)		
Cash and cash equivalents	$ 3,897	$ 7,897	$ 64,947
Loans payable	$ 4,435	$ 4,435	$ 4,435
Convertible promissory notes	2,131	—	—
Derivative liability	1,495	—	—
Preferred stock warrant liability	463	—	—
Convertible preferred stock, $0.001 par value; 8,592,826 shares authorized, 8,268,531 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	39,556	—	—
Stockholders’ equity (deficit):			
Preferred stock, $0.001 par value; no shares authorized, issued or outstanding, actual; 5,000,000 shares authorized, no shares issued or outstanding, pro forma and pro forma as adjusted			
Common stock, $0.001 par value; 45,000,000 shares authorized, 691,312 shares issued and outstanding, actual; 100,000,000 shares authorized, 11,246,963 shares issued and outstanding, pro forma; 100,000,000 shares authorized, 24,246,963 shares issued and outstanding, pro forma as adjusted	1	11	24
Additional paid-in-capital	3,593	55,666	112,703
Accumulated deficit	(47,775)	(51,381)	(51,381)
Total stockholders’ (deficit) equity	$(44,181)	$ 4,296	$ 61,346
Total capitalization	$ 1,393	$ 9,393	$ 66,443

The number of common shares shown as issued and outstanding on a pro forma as adjusted basis in the table is based on the number of shares of our common stock outstanding as of December 31, 2014 and excludes:

- 1,328,873 shares of common stock issuable upon the exercise of outstanding stock options as of December 31, 2014, at a weighted average exercise price of $2.54 per share;
- 124,729 shares of common stock issuable upon the exercise of outstanding warrants as of December 31, 2014 at a weighted-average exercise price of $4.81 per share; and
- 1,155,897 shares of common stock reserved for future issuance under our 2015 Equity Plan (including 405,897 shares of common stock reserved for issuance under our previously existing 2014 Plan, which shares will be added to the shares reserved under the 2015 Equity Plan upon its effectiveness), which will become effective immediately prior to the closing of this offering, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under the 2015 Equity Plan.

Dilution

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the initial public offering price per share and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value (deficit) as of December 31, 2014 was $(45.8) million, or $(66.29) per share of common stock. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our liabilities and convertible preferred stock, which is not included within stockholders' equity (deficit). Historical net tangible book value (deficit) per share is our historical net tangible book value (deficit) divided by the number of shares of common stock outstanding as of December 31, 2014.

Our pro forma net tangible book value as of December 31, 2014 was $2.6 million, or $0.24 per share of common stock. Pro forma net tangible book value represents total tangible assets less total liabilities. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of shares outstanding as of December 31, 2014, after giving effect to (i) the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 8,268,531 shares of common stock immediately prior to the closing of this offering, (ii) the related reclassification of the preferred stock warrant liability to additional paid-in-capital and (iii) the conversion of our September 2014 and February 2015 convertible promissory notes and 184 days and 41 days, respectively, of accrued interest thereon into 2,287,120 shares of our common stock and the resulting loss on extinguishment of $3.6 million based on the initial public offering price of $5.00 per share, in each case, immediately prior to the closing of this offering.

Pro forma as adjusted net tangible book value is our pro forma net tangible book value, after giving further effect to the sale of 13,000,000 shares of our common stock in this offering at the initial public offering price of $5.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. This amount represents an immediate increase in pro forma as adjusted net tangible book value of $2.29 per share to our existing stockholders and an immediate dilution of $2.47 per share to new investors participating in this offering. We determine dilution per share to new investors by subtracting pro forma as adjusted net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Initial public offering price per share		$5.00
Historical net tangible book value (deficit) per share as of December 31, 2014	($66.29)	
Pro forma increase per share	66.53	
Pro forma net tangible book value per share as of December 31, 2014	$ 0.24	
Increase in pro forma as adjusted net tangible book value per share attributable to new investors participating in this offering	$ 2.29	
Pro forma as adjusted net tangible book value per share after this offering		2.53
Dilution per share to new investors participating in this offering		$2.47

If the underwriters fully exercise their option to purchase additional 1,950,000 shares of our common stock in this offering, the pro forma as adjusted net tangible book value will increase to $2.69 per share, representing an immediate increase to existing stockholders of $0.16 per share and an immediate dilution of $2.31 per share to new investors participating in this offering.

The following table summarizes, as of December 31, 2014, on a pro forma as adjusted basis described above, the differences between the number of shares of common stock purchased from us, the total consideration paid to us and the average price per share paid by existing stockholders and by new investors participating in this offering. The calculation below is based on the initial public offering price of $5.00 per share, before deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares Purchased		Total Consideration[1]		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders[2]	11,246,963	46%	$ 49,205,700	43%	$ 4.38
New investors[2]	13,000,000	54%	$ 65,000,000	57%	$ 5.00
Total	24,246,963	100%	$114,205,700	100%	

(1) Total consideration excludes interest accrued on our convertible promissory notes issued in September 2014 and February 2015.
(2) Certain of our existing institutional investors have agreed to purchase an aggregate of 2,700,000 shares of our common stock in this offering at the initial public offering price. The presentation in this table regarding ownership by existing stockholders does not give effect to any purchases in this offering by such investors. See the footnotes to the beneficial ownership table in “Principal Stockholders” for more details.

The number of shares purchased by existing stockholders shown on a pro forma as adjusted basis in the table above and described in the foregoing discussion is based on the number of shares of our common stock outstanding as of December 31, 2014 and excludes:

- 1,328,873 shares of common stock issuable upon the exercise of outstanding stock options as of December 31, 2014, at a weighted average exercise price of $2.54 per share;
- 124,729 shares of common stock issuable upon the exercise of outstanding warrants as of December 31, 2014 at a weighted-average exercise price of $4.81 per share; and
- 1,155,897 shares of common stock reserved for future issuance under our 2015 Equity Plan (including 405,897 shares of common stock reserved for issuance under our previously existing 2014 Plan, which shares will be added to the shares reserved under the 2015 Equity Plan upon its effectiveness), which will become effective immediately prior to the closing of this offering, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under the 2015 Equity Plan.

Selected Financial Data

The selected statement of operations data for the years ended December 31, 2012, 2013 and 2014 and the selected balance sheet data as of December 31, 2013 and 2014 are derived from our audited financial statements appearing elsewhere in this prospectus.

The following selected financial data should be read together with our financial statements and related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" appearing elsewhere in this prospectus. The selected financial data in this section are not intended to replace our financial statements and the related notes. Our historical results are not necessarily indicative of the results that may be expected in the future.

	Year Ended December 31,		
	2012	2013	2014
	(in thousands, except share and per share amounts)		
Statement of Operations Data:			
License revenue	$ 1,538	$ 415	$ 29
Operating expenses:			
Research and development	1,959	4,229	8,294
General and administrative	1,412	1,402	3,412
Total operating expenses	3,371	5,631	11,706
Loss from operations	(1,833)	(5,216)	(11,677)
Other income (expense), net			
Interest income	1	2	2
Interest expense	(256)	(405)	(1,082)
Other income (expense), net	35	(59)	(602)
Total other income (expense)	(220)	(462)	(1,682)
Net loss	$ (2,053)	$ (5,678)	$ (13,359)
Net loss attributable to common stockholders	$ (2,164)	$ (5,678)	$ (13,359)
Net loss per share attributable to common stockholders, basic and diluted[1]	$ (5.14)	$ (13.42)	$ (21.81)
Weighted average common shares outstanding, basic and diluted[1]	421,152	423,059	612,525
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)[2]			$ (1.46)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)[2]			10,147,150

(1) See Note 2 to our financial statements appearing elsewhere in this prospectus for further details on the calculation of basic and diluted net loss per share attributable to common stockholders.

(2) The calculations for the unaudited pro forma net loss per share attributable to common stockholders, basic and diluted, assume: (i) the automatic conversion of all of our outstanding shares of convertible preferred stock into shares of our common stock, as if the conversion had occurred at January 1, 2014, or as of the issuance date of the convertible preferred stock, if later; (ii) the conversion of all of our warrants exercisable for convertible preferred stock into warrants exercisable for shares of our common stock; and (iii) the conversion of our September 2014 convertible promissory notes and 94 days of accrued interest thereon into 1,266,094 shares of common stock and the resulting loss on extinguishment of $2.5 million based on the initial public offering price of $5.00 per share. See Note 2 to our financial statements appearing elsewhere in this prospectus.

	Year Ended December 31, 2013	2014
Balance Sheet Data:		
Cash and cash equivalents	$ 9,781	$ 3,897
Working capital	5,960	(2,506)
Total assets	10,105	6,644
Loans payable	3,063	4,435
Convertible promissory notes	—	2,131
Derivative liability	—	1,495
Preferred stock warrant liability	184	463
Convertible preferred stock	39,556	39,556
Accumulated deficit	(34,416)	(47,775)
Total stockholders' deficit	(33,708)	(44,181)

Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of financial condition and results of operations should be read in conjunction with "Selected Financial Data" and our financial statements and related notes appearing elsewhere in this prospectus. This discussion and analysis and other parts of this prospectus contain forward-looking statements based upon current beliefs, plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under "Risk Factors" and elsewhere in this prospectus. You should carefully read the "Risk Factors" section of this prospectus to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section entitled "Special Note Regarding Forward-Looking Statements."

Overview

We are a clinical-stage specialty pharmaceutical company focused on the development and commercialization of novel and proprietary combination therapies that address significant unmet medical needs. Our initial focus is on the development of Hydros-TA, our proprietary, potentially best-in-class intra-articular, or IA, injectable product candidate to treat pain associated with osteoarthritis, or OA, of the knee. Hydros-TA is a combination IA product designed to provide both rapid and sustained pain relief. We believe the low dose steroid component of Hydros-TA will provide rapid pain relief as well as sustained pain relief up to six months, from our proprietary hyaluronic acid component. Hydros-TA is currently being studied in a Phase 3 trial, which we refer to as COR1.1. We expect to initiate our second Phase 3 trial, which we refer to as COR1.2, to open an investigational new drug application, or IND, and begin enrolling U.S. patients in mid-2015. We anticipate reporting top-line results from COR1.1 in early 2016 and COR1.2 by the end of 2016, and submitting our NDA for Hydros-TA in early 2017.

Since our inception, we have devoted substantially all our efforts and financial resources to identifying and developing product candidates utilizing our proprietary hyaluronic acid technology and to the clinical development of Hydros-TA. We have not generated any revenue from product sales and, as a result, we have incurred significant losses. Through December 31, 2014, we have funded substantially all of our operations through the sale and issuance of our convertible preferred stock and convertible promissory notes and through various credit facilities.

In November 2012, we entered into a technology license agreement with Shanghai Jingfeng Pharmaceutical Co., Ltd., or Jingfeng, pursuant to which we granted to Jingfeng an exclusive license to develop, manufacture and commercialize Hydros-TA in China, Taiwan, Hong Kong and Macau. In consideration for the exclusive license, we received a non-refundable up-front payment of $2.0 million ($1.7 million net of Chinese withholding tax). Additionally, we are eligible to receive future regulatory milestone payments of up to $1.5 million, which are considered non-substantive milestones for accounting purposes, and commercialization royalty payments of up to approximately $5.0 million (each excluding Chinese withholding tax).

Other than our arrangement with Jingfeng, we own global development and commercialization rights to Hydros-TA. Upon FDA approval, we expect to commercialize Hydros-TA for OA pain in the knee in the United States with an approximately 50 to 100 person specialty sales force targeting orthopedic surgeons, rheumatologists and pain specialists.

We do not have manufacturing facilities and all of our manufacturing activities are contracted out to third parties. Additionally, we currently utilize third-party clinical research organizations, or CROs, to carry out our clinical trials and we do not yet have a sales organization. We expect to significantly increase our investment in costs relating to our clinical and commercial manufacturing process and inventory of Hydros-TA as we progress through our Phase 3 clinical trials and prepare for a possible commercial launch of Hydros-TA.

We will need substantial additional funding to support our operating activities, as we increase our clinical activities and approach commercial launch in the United States. Adequate funding may not be available to us on acceptable terms, or at all. In its report accompanying our audited financial statements for the year ended December 31, 2014, our independent registered public accounting firm included an explanatory paragraph stating that our recurring losses from operations and our need for additional sources of capital to fund our ongoing operations raise substantial doubt as to our ability to continue as a going concern. A report with this type of explanatory paragraph could impair our ability to finance our operations through the sale of debt or equity securities or to obtain commercial bank financing. Our ability to continue as a going concern will depend, in large part, on our ability to obtain necessary financing, which is uncertain. Our failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on our business, results of operations and financial condition. In September 2014 and February 2015, we issued convertible promissory notes in an aggregate principal amounts of $5.0 million and $4.0 million, respectively, to certain of our existing investors. These promissory notes will automatically convert into shares of our common stock in connection with this offering at a price equal to 80% of the initial public offering price of a share of our common stock.

We have never been profitable and, as of December 31, 2014, we had an accumulated deficit of $47.8 million. We incurred net losses of approximately $2.2 million, $5.7 million and $13.4 million in the years ended December 31, 2012, 2013 and 2014, respectively. We expect to continue to incur net operating losses as we advance Hydros-TA through clinical development, seek regulatory approval and prepare for and, if approved, proceed to commercialization.

Financial Overview

Revenue

We do not have any products approved for sale, and we have not generated any revenue from product sales since our inception and do not expect to generate any revenue from the sale of products in the near future. We may generate revenue from product sales, license fees, milestone payments and royalties from the sale of products developed using our intellectual property in the future. Our ability to generate revenue and become profitable depends on our ability to successfully commercialize Hydros-TA and any other product candidates that we may advance. If we fail to complete the development of, or obtain regulatory approval for, Hydros-TA or any future product candidates we may advance, our ability to generate future revenue and our results of operations and financial position will be adversely affected.

Our revenue to date has been generated from license revenue pursuant to our agreement with Jingfeng. Revenue under our license arrangement is recognized based on the performance requirements of the contract. Determinations of whether persuasive evidence of an arrangement exists and whether delivery has occurred or services have been rendered are based on management's judgments regarding the fixed nature of the fees charged for deliverables and the collectability of those fees. Should changes in conditions cause management to determine that these criteria are not met for any new or modified transactions, revenue that we are able to recognize could be adversely affected. We have identified all of the deliverables at the inception of the Jingfeng agreement, including an exclusive royalty bearing license to certain of our patents relating to Hydros-TA, know-how and reasonable professional services, clinical or nonclinical data and information, collectively referred to as services, to be provided by us to assist Jingfeng in manufacturing, developing and commercializing the licensed product over the performance period, which is currently estimated to be January 2019. We have determined that the Jingfeng license and the services thereunder, represent two separate units of accounting, as the license has standalone value apart from the services because the development, manufacturing and commercialization rights conveyed would allow Jingfeng to perform all efforts necessary to bring the product to commercialization and begin selling the product upon regulatory approval. Non-substantive regulatory milestone and commercialization royalty payments are recognized in proportion to the two units of accounting identified at the inception of the agreement. Each portion will be recognized in accordance with the underlying unit of accounting.

We determined the best estimate of selling price, or BESP, for the license unit of accounting using a discounted cash flow analysis. This measurement is based on the value indicated by current estimates of future payments to be received under the agreement and reflects management determined estimates and assumptions. These estimates and assumptions include but are not limited to estimated sales prices, estimated market opportunity, expected market share, the likelihood that clinical trials will be successful, the likelihood that regulatory approval will be received, the likelihood that the products will be commercialized, the determination of the markets served and the discount rate. We reduced the future payment to be received by the estimated amount of the professional services costs plus an estimated margin, which was based on industry benchmarking of similar companies. These estimates and assumptions formed the basis of an expected net future cash flow that was discounted based on an estimated weighted average cost of capital. The BESP for the services unit of accounting was determined using a similar methodology. This measurement is based on the estimated cost of the professional services plus an estimated margin based on industry benchmarking of similar companies.

The considerations of the Jingfeng agreement have been allocated to the units of accounting based on the relative selling price method. Of the $1.7 million up-front payment received (net of Chinese withholding tax), $1.5 million was allocated to the license and $0.1 million to the services. We recognized license revenue upon execution of the agreement as the associated unit of accounting had been delivered pursuant to the terms of the agreement. The $0.1 million allocated to services will be recognized as revenue on a straight-line basis over the performance period, which is currently estimated to be January 2019.

In November 2013, we received a $0.4 million regulatory milestone payment (net of Chinese withholding tax), and all but $35,000 was allocated to the license. We recognized license revenue upon execution of the agreement as the associated unit of accounting had been delivered pursuant to the terms of the agreement. The $35,000 allocated to services will be recognized as revenue on a straight-line basis over the performance period, which is currently estimated to be January 2019.

We expect that any revenue we generate will fluctuate from year to year as a result of the timing and amount of milestone payments from our license agreement with Jingfeng and any future collaboration partner.

Operating Expenses

Most of our operating expenses to date have been related to the research and development activities of Hydros-TA.

Research and Development Expenses. Since our inception, we have focused our resources on our research and development activities, including nonclinical and pre-clinical studies, clinical trials and chemistry manufacturing and controls. Our development expenses consist primarily of:

- expenses incurred under agreements with consultants, CROs and investigative sites that conduct our pre-clinical studies and clinical trials;
- costs of acquiring, developing and manufacturing clinical trial materials;
- personnel costs, including salaries, benefits, stock-based compensation and travel expenses for employees engaged in scientific research and development functions;
- costs related to compliance with regulatory requirements; and
- allocated expenses for rent and maintenance of facilities, insurance and other general overhead.

Research and development costs are expensed as incurred. Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as subject enrollment, clinical site activations or information provided to us by our third-party vendors.

We do not currently utilize a formal time allocation system to capture expenses on a project-by-project basis, as the majority of our past and planned expenses have been and will be in support of Hydros-TA. We expect to increase our research and development expenses for the foreseeable future as we initiate further clinical trials.

The following table summarizes our research and development expenses by functional area:

	Year Ended December 31,		
	2012	2013	2014
	(in thousands)		
Clinical development	$ 61	$ 893	$2,804
Regulatory	37	213	392
Pre-clinical R&D	650	614	1,108
Personnel related	1,042	1,185	2,345
Manufacturing	169	1,324	1,645
Total research and development expenses	$1,959	$4,229	$8,294

It is difficult to determine with any certainty the duration and completion costs of our currently planned or future clinical trials of Hydros-TA and any future product candidates we may advance, or if, when or to what extent we will generate revenue from the commercialization and sale of Hydros-TA or future product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including the uncertainties of future clinical trials and pre-clinical studies, uncertainties in clinical trial enrollment rate and significant and changing government regulation. In addition, the probability of success for each product candidate will depend on numerous factors, including competition, manufacturing capability and commercial viability.

General and administrative expenses. General and administrative expenses consist of personnel costs, travel expenses and other expenses for outside professional services, including legal, human resources, audit and accounting services. Personnel costs consist of salaries, bonus, benefits and stock-based compensation. We expect to incur additional expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, Nasdaq listing standards, additional insurance expenses, investor relations activities and other administration and professional services. General and administrative expenses are expensed as incurred.

For the years ended December 31, 2012, 2013 and 2014 our general and administrative expenses totaled approximately $1.4 million, $1.4 million and $3.4 million, respectively. We anticipate that our general and administrative expenses will increase in the future as we continue to build our corporate infrastructure to support the continued development of Hydros-TA.

Other Income (Expense), Net

Interest income. Interest income consists of interest earned on our cash and cash equivalents balances. The primary objective of our investment policy is capital preservation. We anticipate that our interest income will increase in the future due to our receipt of the anticipated net proceeds from this offering.

Interest expense. Interest expense consists of interest expense on amounts outstanding under our debt facility with Silicon Valley Bank, or SVB, as well as non-cash interest expense related to the amortization of debt discounts and final interest payments. We expect to incur future interest expense related to this borrowing until June 2018. See “— Liquidity and Capital Resources” for a more detailed description of our credit facility.

Other income (expense), net. Other income (expense), net primarily consists of changes in the estimated fair value of the convertible preferred stock warrants.

Income Taxes

We account for income taxes under the asset and liability method. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amounts expected to be realized.

Our deferred tax assets do not include the excess tax benefit related to stock-based compensation that are a component of our federal and state net operating loss carryforwards in the amount of $0.3 million as of December 31, 2014. The excess tax benefit reflected in our net operating loss carryforwards will be accounted for as a credit to stockholders' equity, if and when realized. In determining if and when excess tax benefits have been realized, we have elected to utilize the with-and-without approach with respect to such excess tax benefits. We have also elected to ignore the indirect tax effects of stock-based compensation deductions for financial and accounting reporting purposes, and specifically to recognize the full effect of the research tax credit in income from operations.

As of December 31, 2014, we had net operating loss, or NOL, carryforwards for federal income tax purposes of approximately $44.2 million that expire beginning in 2024 if not utilized, and federal research and development tax credit carryforwards of approximately $0.6 million that expire beginning in 2026 if not utilized. In addition, we had NOL carryforwards for state income tax purposes of approximately $43.8 million that expire beginning in 2026 if not utilized, and state research and development tax credit carryforwards of approximately $0.5 million, which do not expire.

Utilization of the NOL and tax credit carryforwards may be subject to substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code and similar state provisions. Such an annual limitation could result in the expiration of the NOL and tax credit carryforwards before their utilization. In general, if we experience a greater than 50 percentage point aggregate change (by value) in the equity ownership of certain stockholders over a rolling three-year period (a Section 382 ownership change), utilization of our pre-change NOL carryforwards are subject to an annual limitation under Section 382 of the Internal Revenue Code (California has similar laws). Such limitations may result in expiration of a portion of the NOL carryforwards before utilization. We have determined that an ownership change occurred in December 2005, which resulted in a permanent loss of $287,000 of the federal net operating losses carryforwards. Our ability to use our remaining NOL carryforwards may be further limited if we experience a Section 382 ownership change in connection with this offering or as a result of future changes in our stock ownership.

Results of Operations

Comparison of the Years Ended December 31, 2013 and 2014

The following table summarizes our results of operations for the years ended December 31, 2013 and 2014:

	Year Ended December 31,		Change
	2013	2014	
	(in thousands)		
License revenue	$ 415	$ 29	$ (386)
Operating expenses:			
Research and development	4,229	8,294	4,065
General and administrative	1,402	3,412	2,010
Total operating expenses	5,631	11,706	6,075
Loss from operations	(5,216)	(11,677)	(6,461)
Other income (expense), net:			
Interest income	2	2	0
Interest expense	(405)	(1,082)	(677)
Other income (expense), net	(59)	(602)	(543)
Total other income (expense)	(462)	(1,682)	(1,220)
Net loss	$(5,678)	$(13,359)	$(7,681)
Net loss attributable to common stockholders	$(5,678)	$(13,359)	$(7,681)

License revenue

Revenues for the years ended December 31, 2013 and 2014 were $0.4 million and $29,000 respectively, in each period. We received the $0.4 million from Jingfeng in November 2013 upon the successful production by Jingfeng of the first batch of Hydros-TA, and the $29,000 is related to the amortization of deferred revenue associated with the Jingfeng agreement.

Research and development expenses

Research and development expenses were $4.2 million and $8.3 million for the years ended December 31, 2013 and 2014, respectively. The increase in research and development expenses period over period of $4.1 million, or 98%, was primarily due to the following:

- an increase in clinical development expenses of $1.9 million as we began enrolling patients in our first Phase 3 clinical trial, COR1.1, beginning in January 2014;
- an increase in pre-clinical research and development expenses of $0.5 million primarily related to the increased use of CROs and other outside services driven by an increase in IND enabling activities;
- an increase in personnel related expenses of $1.2 million as we began to build out our in-house regulatory and clinical development team; and
- an increase in manufacturing related expenses of $0.3 million, primarily related to an increased use of contract manufacturers in preparation for the production of Hydros-TA as we began to produce materials for our COR1.2 clinical trial.

General and administrative expenses

General and administrative expenses were $1.4 million and $3.4 million for the years ended December 31, 2013 and 2014, respectively. The increase in general and administrative expenses period over period of

$2.0 million, or 143%, was primarily due to an increase of $0.3 million in salary and related costs due to an increase in bonus accrual as compared to the prior period, an increase of $0.2 million based on an increased use of outside consulting services and an increase of $1.3 million in professional fees.

Interest expense

Interest expense is attributable to our debt facility with SVB and non-cash amortization of debt discounts and final interest payments. Interest expense was $0.4 million and $1.1 million for the years ended December 31, 2013 and 2014, respectively. The increase in interest expense of $0.7 million was primarily due to expense of the unamortized portion of the final interest payment related to the loan and security agreement with SVB.

Other income (expense), net

Other income (expense), net was $(59,000) and $(0.6) million for the years ended December 31, 2013 and 2014, respectively. The increase in expense of $0.5 million was based primarily on an increase in the fair value of the warrant liability of $0.3 million and our increase in the fair value of the derivative liability of $0.4 million.

Comparison of the Years Ended December 31, 2012 and 2013

The following table summarizes our results of operations for the years ended December 31, 2012 and 2013:

	Year Ended December 31,		Change
	2012	2013	
	(in thousands)		
License revenue	$ 1,538	$ 415	$(1,123)
Operating expenses:			
Research and development	1,959	4,229	2,270
General and administrative	1,412	1,402	(10)
Total operating expenses	3,371	5,631	2,260
Loss from operations	(1,833)	(5,216)	(3,383)
Other income (expense), net:			
Interest income	1	2	1
Interest expense	(256)	(405)	(149)
Other income (expense), net	35	(59)	(94)
Total other income (expense)	$ (220)	$ (462)	$ (242)
Net loss	$(2,053)	$(5,678)	$(3,625)
Net loss attributable to common stockholders	$(2,164)	$(5,678)	$(3,514)

License revenue

Revenues for the years ended December 31, 2012 and 2013 were $1.5 million and $0.4 million, respectively. The decrease of $1.1 million, or 73%, was primarily due to the recognition of $1.5 million in up-front licensing fees received from Jingfeng upon signing of the agreement in November 2012, compared to the $0.4 million we received from Jingfeng in November 2013 upon the successful production by Jingfeng of the first batch of Hydros-TA.

Research and development expenses

Research and development expenses were $2.0 million and $4.2 million for the years ended December 31, 2012 and 2013, respectively. The increase in research and development expenses period over period of $2.2 million, or 110%, was primarily due to the following:

- an increase in clinical development expenses of $0.8 million as we began to incur increased costs related to the increased use of CROs and increase site initiation costs in anticipation of beginning COR1.1 in January 2014;
- an increase in regulatory expenses of $0.2 million primarily related to the increased use of consultants and other outside services driven by an increase in IND enabling activities;
- an increase in manufacturing related research and development expenses of $1.2 million driven by our increased use of contract manufacturers related to the production of our clinical trial materials for COR1.1; and
- an increase in personnel related expenses of $0.1 million as we began to build out our in-house regulatory and clinical development team.

General and administrative expenses

General and administrative expenses were $1.4 million for the year ended December 31, 2012, which was comparable to general and administrative expenses of $1.4 million for the year ended December 31, 2013.

Interest expense

Interest expense is primarily attributable to our debt facility with SVB and non-cash amortization of debt discounts and final interest payments. Interest expense for the years ended December 31, 2012 and 2013 was $0.3 million and $0.4 million, respectively. The increase in interest expense of $0.1 million was primarily driven by the $0.2 million in the acceleration of the final interest payment amortization associated with the February 2013 amendment to the SVB debt facility.

Other income (expense), net

Other income (expense), net was $35,000 and ($59,000) for the years ended December 31, 2012 and 2013, respectively. The increase in expense of $94,000 was based primarily on an increase in the fair value of the warrant liability of $63,000.

Liquidity and Capital Resources

To date, we have not generated any revenue and have incurred losses since our inception in 2004. As of December 31, 2014, we had an accumulated deficit of $47.8 million. We anticipate that we will continue to incur losses for the foreseeable future. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may seek to obtain through one or more equity offerings, debt financings, government or other third-party funding and licensing or collaboration arrangements.

Since our inception through December 31, 2014, we have funded our operations principally through the receipt of funds from private placements of our equity, the issuance of convertible promissory notes and borrowings under our loan and security agreement with SVB. As of December 31, 2014, we had cash and cash equivalents of $3.9 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to capital preservation.

In order to continue operations, we must raise additional equity or debt financings and achieve profitable operations. Although we have been successful in raising capital in the past, there can be no assurance that we will be able to obtain additional equity or debt financing on acceptable terms, or at all. The failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect our business, results of operations, future cash flows and financial condition. Since our inception, we have generated significant losses and expect to continue to generate losses for the foreseeable future. Our independent registered public accounting firm has expressed in its report on our financial statements included as part of this prospectus a "going concern" opinion, meaning that we have suffered recurring losses from operations and negative cash flows from operations that raise substantial doubt regarding our ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. We believe that our available cash, together with the proceeds from this offering will be sufficient to satisfy our liquidity requirements for at least the next 12 months. We have utilized, and may continue to utilize, debt arrangements with debt providers and financial institutions to finance our operations. Factors such as interest rates and available cash will impact our decision to continue to utilize debt arrangements as a source of cash.

Indebtedness

In October 2011, we entered into a loan and security agreement with SVB that provided for us to borrow $3.0 million. Upon the drawdown of the $3.0 million, we issued a warrant to purchase 21,739 shares of Series B convertible preferred stock. Interest only payments were required through July 2012, and the principal amount of the loan was repayable in 36 equal monthly installments plus accrued interest beginning August 2012. The interest rate on the loan was 5.15% per annum. In addition, the loan and security agreement allowed us to borrow another $2.0 million, contingent on certain conditions.

In July 2012, we entered into a first amendment to the loan and security agreement to extend the commitment period for the additional $2.0 million through November 2012. We did not draw on the second term loan for $2.0 million. We amended the original warrant agreement and issued a warrant to purchase 14,493 shares of series B convertible preferred stock. In connection with a change in liquidation preference due to the Series B convertible preferred stock financing, a warrant to purchase 5,344 shares of Series B convertible preferred stock was issued to SVB. In February 2013, we entered into a second amendment to the loan and security agreement to provide for a new loan of $3.0 million and repayment of the outstanding principal of the original loan entered into October 2011, with the remaining proceeds provided to us. We also amended the original warrant agreement and issued a warrant to purchase 8,316 shares of Series B convertible preferred stock, as well as issuing a separate warrant to purchase 24,946 shares of Series B convertible preferred stock. The interest rate was 3.25% per annum and the loan was repayable in 30 equal monthly installments, following a ten-month interest only period. Additionally, the amendment provided the terms for a second loan for $1.3 million that would be available through November 2013, contingent on certain conditions.

In December 2013, we entered with a third amendment to the loan and security agreement to extend the commitment date for the loan of $1.3 million to January 31, 2014, to extend the interest only period for four additional months and reduce the number of payments to 29 equal monthly installments if the new loan was drawn. In January 2014, we drew the second loan of $1.3 million and issued a warrant to purchase 10,394 shares of Series B convertible preferred stock. The interest rate was 3.59% per annum and the loan was repayable in 29 equal monthly installments, following a four-month interest only period. The interest only period expired in May 2014 and we began paying principal and interest payments of $0.2 million per month.

In September 2014, we entered into a fourth amendment to the loan and security agreement to provide for a new loan of $4.5 million and repayment in full of amounts owing under the prior loans, with net proceeds to us of $0.5 million. We also issued a warrant to purchase 18,709 shares of Series B convertible preferred stock. The interest rate is 3.95% per annum and the loan is repayable in 36 equal monthly installments, following a nine month interest-only period. The amendment provides for an extension of the interest-only period by an additional nine months, to March 2016, under certain conditions, including if we raise at least $30.0 million in this offering.

The loan and security agreement is collateralized by our personal property but excludes our intellectual property. The agreement also contains customary representations and warranties, covenants, closing and advancing conditions, events of defaults and termination provisions. The negative covenants preclude, among other things, disposing of certain assets, engaging in any merger or acquisition, incurring additional indebtedness, encumbering any collateral or making prohibited investments, in each case, without the prior consent of the SVB.

The loan and security agreement provides that an event of default will occur if, among other events, we default in the payment of any amount payable under the agreement when due. As of December 31, 2013 and December 31, 2014, we were in compliance with all the covenants in the loan and security agreement.

On September 29, 2014 and February 19, 2015, we entered into a convertible note purchase agreement and issued convertible promissory notes (collectively, the "Notes") in an aggregate principal amount of $5.0 million and $4.0 million, respectively, to several related parties that own more than 10% of our capital stock. Upon completion of our initial public offering, the Notes will automatically convert into a number of shares of our common stock equal to the quotient obtained by dividing the entire principal amount and accrued interest on the convertible promissory notes by 80% of the initial public offering price per share of our common stock. If we, prior to the completion of an initial public offering, issue a next series equity financing with proceeds of at least $10,000,000, excluding conversion of the Notes, then the Notes will automatically convert into the shares of the next equity series. The number of shares of our common stock at this conversion will be equal to the quotient obtained by dividing the entire principal amount and accrued interest on the Notes by 80% of the next equity series financing price per share. In the event that we do not complete an initial public offering or a next series equity financing on or before June 30, 2015, if holders of at least a majority of the principal amount of the then-outstanding Notes elect to convert the Notes, rather than electing to have the Notes repaid in cash following the maturity date of December 31, 2015, the conversion must be into shares of the Series B convertible preferred stock.

In the event that we sell or disposes of all or substantially all of its property or business or merges or consolidates with any other entity (other than its wholly-owned subsidiary) prior to the repayment or conversion of the Notes, holders of the Notes will be paid an amount equal to 120% of the outstanding principal amount, together with any accrued interest, so long as our indebtedness under the Loan and Security Agreement has been paid in full.

The Notes bear interest at a rate of 5% per annum, compounded annually. Unless converted, the Notes will mature upon the demand by holders of at least a majority of the principal amount of the then-outstanding notes at any time on or after December 31, 2015, but in no event before our indebtedness under the Loan and Security Agreement has been paid in full.

Cash Flows

The following table shows a summary of our cash flows for each of the years ended December 31, 2012, 2013 and 2014:

	Year Ended December 31,		
	2012	2013	2014
	(in thousands)		
Cash flows used in operating activities	$(1,835)	$(4,858)	$(11,253)
Cash used in investing activities	(91)	(18)	(159)
Cash flows provided by financing activities	5,564	6,415	5,528
Net increase (decrease) in cash and cash equivalents	3,638	1,539	(5,884)

Operating Activities. Operating activities used $1.8 million of cash in 2012. The cash flow used in operating activities resulted primarily from our net loss of $2.1 million for the year, offset by net non-cash charges of

$0.2 million. Our non-cash charges consisted primarily of $0.1 million related to non-cash interest expense and $47,000 related to stock based compensation.

Operating activities used $4.9 million of cash in 2013. The cash flow used in operating activities resulted primarily from our net loss of $5.7 million for the year, offset by net non-cash charges of $0.4 million and net cash provided by changes in our operating assets and liabilities of $0.5 million. Our non-cash charges consisted primarily of $63,000 related to the change in fair value of preferred stock warrant liability, $0.2 million related to stock-based compensation expense and $32,000 related to non-cash interest expense. Net cash provided by changes in our operating assets and liabilities consisted primarily of a $0.3 million increase in our accounts payable and $0.2 million increase in accruals.

Operating activities used $11.3 million of cash in 2014. The cash flow used in operating activities resulted primarily from our net loss of $13.4 million for the period, offset by net non-cash charges of $1.5 million and net cash provided by changes in our operating assets and liabilities of $0.6 million. Our non-cash charges consisted primarily of $0.6 million related to an increase in the fair value of the preferred stock warrant liability and derivative liability, $0.4 million related to stock-based compensation expense and $0.4 million related to the amortization of our convertible debt discount. Net cash provided by changes in our operating assets and liabilities consisted primarily of a $0.5 million increase in our accounts payable and a $0.8 million increase in accruals, offset by a decrease in prepaid expenses of $0.6 million and a decrease in other assets of $0.1 million.

Investing activities. Net cash used in investing activities was $91,000, $18,000 and $0.2 million in the years ended December 31, 2012, 2013 and 2014, respectively. Net cash used in investing activities consisted primarily of cash paid to purchase property and equipment.

Financing activities. Net cash provided by financing activities was $5.6 million, $6.4 million and $5.5 million in the years ended December 31, 2012, 2013 and 2014, respectively. Net cash provided by financing activities in the year ended December 31, 2012 primarily consisted of $6.0 million from the sale of Series B preferred stock, net of issuance costs, offset by $0.4 million used in the repayment of a loan. Net cash provided by financing activities in the year ended December 31, 2013 primarily consisted of $6.0 million received from the sale of Series B preferred stock, net of issuance costs, net proceeds of $0.5 million from a $3.0 million loan payable and $2.5 million loan payoff, which was offset by $0.2 million related to repayment of a loan. Net cash provided by financing activities in the year ended December 31, 2014 consisted of the receipt of $5.0 million from the issuance of convertible promissory notes, the receipt of net proceeds of $2.2 million from loans payable and $0.2 million from the issuance of common stock related to option exercise, partially offset by the repayment of $0.7 million in existing borrowings and $1.2 million in deferred costs associated with this initial public offering.

Future Funding Requirements

To date, we have not generated any revenue from product sales, and we do not know when, or if, we will generate any revenue from product sales. We do not expect to generate any revenue from product sales unless and until we obtain regulatory approval of and commercialize Hydros-TA or any future product candidates that we may advance. At the same time, we expect our expenses to increase in connection with our ongoing development activities, particularly as we continue the development and clinical trials of, and seek regulatory approval for, Hydros-TA. Upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. In addition, subject to obtaining regulatory approval of any product candidate, we expect to incur significant commercialization expenses for product sales, marketing and manufacturing. We anticipate that we will need substantial additional funding in connection with our continuing operations.

Based upon our current operating plan, we believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital requirements for at least the next 12 months. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and

uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development and commercialization of our product candidates.

Our future capital requirements will depend on many factors, including:

- the progress, rate of enrollment, timing, scope, results and costs of our nonclinical and clinical trials for Hydros-TA, including the ability to enroll patients in a timely manner for clinical trials;
- the time and cost necessary to obtain regulatory approvals for Hydros-TA and the costs of post-marketing studies that could be required by regulatory authorities;
- our ability to successfully commercialize Hydros-TA;
- the manufacturing, selling and marketing costs associated with Hydros-TA, including the cost and timing of building our sales and marketing capabilities;
- our ability to establish and maintain collaboration partnerships, in-license/out-license or other similar arrangements and the financial terms of such agreements;
- the scope of our research and clinical development activities to expand the use of Hydros-TA for treating OA in other joints;
- the sales price and the availability of adequate third-party reimbursement for Hydros-TA;
- the cash requirements of any future acquisitions or discovery of future product candidates;
- the number and scope of nonclinical, pre-clinical and discovery programs that we decide to pursue or initiate;
- the time and cost necessary to respond to technological and market developments; and
- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of Hydros-TA or any other future product candidates.

Until such time, if ever, as we can generate substantial revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, government or other third-party funding and licensing or collaboration arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through government or other third-party funding, marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2014:

	Payments Due By Period				
	Total	Less Than 1 Year	1 – 3 Years	3 – 5 Years	More Than 5 Years
	(in thousands)				
Loans payable (including interest)[1]	$ 5,375	$ 1,005	$3,190	$1,180	—
Convertible promissory notes (including interest)[2]	5,316	5,316		—	—
Operating lease obligations[3]	511	438	73	—	—
Total[4]	$11,202	$ 6,759	$3,263	$1,180	—

(1) Represents the contractually required principal and interest payments on our credit facility in accordance with the required payment schedule. Amounts associated with future interest payments to be made were calculated using a weighted average interest rate of 10.2% per annum.

(2) Represents the contractually required payments under our convertible promissory notes in existence as of December 31, 2014. Amounts associated with the future interest payments to be made were calculated using the stated rate of 5% and an assumed maturity date of December 31, 2015.

(3) Represents the contractually required payments under our operating lease obligations in existence as of December 31, 2014 in accordance with the required payment schedule. No assumptions were made with respect to renewing the lease terms at the expiration date of their initial terms.

(4) This table does not include a liability for unrecognized tax benefits related to various federal and state income tax matters of $0.6 million at December 31, 2014. The timing of the settlement of these amounts was not reasonably estimable at December 31, 2014. We do not expect payment of amounts related to the unrecognized tax benefits within the next twelve months.

The tables above reflect only payment obligations that are fixed or determinable. We enter into contracts in the normal course of business with CROs for clinical trials and clinical supply manufacturing and with vendors for pre-clinical research studies, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore we believe that our non-cancellable obligations under these agreements are not material.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of our financial statements and the reported revenue and expenses during the reported periods. We evaluate these estimates and judgments, including those described below, on an ongoing basis. We base our estimates on historical experience, known trends and events, contractual milestones and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2 to our financial statements appearing elsewhere in this prospectus, we believe that the estimates and assumptions involved in the following accounting policies may have the greatest potential impact on our financial statements and, therefore, consider these to be critical for fully understanding and evaluating our financial condition and results of operations.

Revenue Recognition

Revenue under our license arrangement is recognized based on the performance requirements of the contract. Determinations of whether persuasive evidence of an arrangement exists and whether delivery has occurred or services have been rendered are based on our judgment regarding the fixed nature of the fees charged for deliverables and the collectability of those fees. Should changes in conditions cause us to determine that these criteria are not met for any new or modified transactions, revenue recognized could be adversely affected.

We recognize revenue related to our license arrangement in accordance with the provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605-25, *Revenue Recognition — Multiple-Element Arrangements*, or ASC Topic 605-25 which provides guidance on how deliverables in an arrangement should be separated and how the arrangement consideration should be allocated to the separate units of accounting:

- requiring an entity to determine the selling price of a separate deliverable using a hierarchy of (i) vendor-specific objective evidence, or VSOE, (ii) third-party evidence, or TPE, or (iii) BESP; and

- requiring the allocation of the arrangement consideration, at the inception of the arrangement, to the separate units of accounting based on relative fair value.

We evaluate all deliverables within an arrangement to determine whether or not they provide value on a stand-alone basis. Based on this evaluation, the deliverables are separated into units of accounting. The arrangement consideration that is fixed or determinable at the inception of the arrangement is allocated to the separate units of accounting based on their relative selling prices. We may exercise significant judgment in determining whether a deliverable is a separate unit of accounting, as well as in estimating the selling prices of such unit of accounting.

To determine the selling price of a separate deliverable, we use the hierarchy as prescribed in ASC Topic 605-25 based on VSOE, TPE or BESP. VSOE is based on the price charged when the element is sold separately and is the price actually charged for that deliverable. TPE is determined based on third-party evidence for a similar deliverable when sold separately and BESP is the price at which we would transact a sale if the elements of collaboration and license arrangements were sold on a stand-alone basis. We may not be able to establish VSOE or TPE for the deliverables within collaboration and license arrangements as we do not have a history of entering into such arrangements or selling the individual deliverables within such arrangements separately. In addition, there may be significant differentiation in these arrangements, which indicates that comparable third-party pricing may not be available. We may determine that the selling price for the deliverables within collaboration and license arrangements should be determined using BESP. The process for determining BESP involves significant judgment on our part and includes consideration of multiple factors such as estimated direct expenses and other costs and available data.

For each unit of accounting identified within an arrangement, we determine the period over which the performance obligation occurs. We allocate the arrangement consideration to the separate units of accounting based on the relative selling prices. Revenue is recognized immediately if the performance obligation has been met. We recognize the revenue that is deferred using the straight-line method over the expected delivery period of the unit of accounting.

Research and Development Costs

As part of the process of preparing our financial statements, we are required to estimate our accrued and prepaid research and development expenses. We review new and open contracts and communicate with applicable internal and vendor personnel to identify services that have been performed on our behalf and estimate the level of service performed and the associated costs incurred for the service when we have not yet been

invoiced or otherwise notified of the actual cost for accrued expenses. In addition, we review and expense contractual liability for which the costs are not recoverable in the event of cancellation. The majority of our service providers invoice us monthly in arrears for services performed; however, some require advanced payments. For any services that require such advanced payments, we perform a review with applicable internal and vendor personnel to estimate the level of services that have been performed and the associated costs that have been incurred at each reporting period.

We base our accrued expenses related to clinical trials on estimates of patient enrollment and related expenses at clinical investigator sites, as well as estimates for services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage clinical trials on our behalf. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we modify our estimates of accrued expenses accordingly on a prospective basis.

If we do not identify costs that we have begun to incur, or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. To date, we have not adjusted our estimates at any particular balance sheet date in any material amount.

Stock-Based Compensation

We maintain performance incentive plans under which incentive stock options and non-qualified stock options may be granted to employees and non-employees. We account for stock-based compensation arrangements with employees in accordance with ASC 718, *Compensation—Stock Compensation*. ASC 718 requires the recognition of compensation expense, using a fair value-based method, for costs related to all share-based payments including stock options. In determining the fair value of the stock-based awards, we use the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected term. The expected term represents the period that the our stock-based awards are expected to be outstanding. We used the average of the expected term as disclosed for comparable publicly traded biopharmaceutical companies as we do not have sufficient experience to estimate the expected term based on historical exercises. The expected term of stock options granted to non-employees is equal to the contractual term of the option award.

Expected volatility. Since we are a privately held company and do not have any trading history for our common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. When selecting comparable publicly traded biopharmaceutical companies on which we have based our expected stock price volatility, we selected companies with comparable characteristics, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Risk-free interest rate. The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected dividend. We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

The fair value of stock option awards to employees was estimated at the date of grant using a Black-Scholes option-pricing model with the following weighted-average assumptions:

	Year Ended December 31,		
	2012	2013	2014
Expected term (in years)	*	5.39	5.39
Expected volatility	*	80.7%	56.0%
Risk-free interest rate	*	0.87 to 1.47%	1.70 to 1.82%
Dividend yield	*	0%	0%

* We did not grant any stock options in the year ended December 31, 2012.

For all periods prior to this initial public offering, the fair values of the shares of common stock underlying our share-based awards were estimated on each grant date by our board of directors. In order to determine the fair value of our common stock underlying option grants, our board of directors considered, among other things, contemporaneous valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Given the absence of a public trading market for our common stock, our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including our stage of development, progress of our research and development efforts, the rights, preferences and privileges of our preferred stock relative to those of our common stock, equity market conditions affecting comparable public companies and the lack of marketability of our common stock.

We considered the following approaches in the preparation of our valuations:

- *Market Approach*. The market approach values a business by reference to guideline companies, for which enterprise values are known.
- *Option-Pricing Method Backsolve, or OPM backsolve*. The OPM backsolve method derives the implied equity value for a company from a recent transaction involving the company's own securities issued on an arm's-length basis.
- *Probability Weighted Approach*. Using the probability weighted approach, the value of a company's common stock is estimated based upon the analysis of future values for the company assuming various possible future liquidity events like an initial public offering, or IPO, or remaining private. Share value is based upon the probability-weighted present value of expected future net cash flows, considering each of the possible future events, as well as the rights and preferences of each share class.

In addition, we also considered an enterprise value allocation method:

- *Option-Pricing Method, or OPM*. Under this method, each class of stock is modeled as a call option with a distinct claim on the enterprise value of the company. The option's exercise prices would be based on a comparison with the enterprise value. The method assumes that a formula, such as the Black-Scholes model, would calculate the fair value when provided with certain values, including share price, expiration date, volatility and the risk free interest rate.

Stock-based compensation expense was $47,000, $0.2 million and $0.4 million for the years ended December 31, 2012, 2013 and 2014, respectively.

For valuations after the completion of this offering, our board of directors will determine the fair value of each share of underlying common stock based on the closing price of our common stock as reported on the date of grant.

The intrinsic value of all outstanding options as of December 31, 2014 was $4.1 million, based on the estimated fair value of our common stock of $5.00 per share, the initial offering price on the cover page of this prospectus.

Estimated Fair Value of Convertible Preferred Stock Warrants

Freestanding warrants for shares that are contingently redeemable are classified as a liability on the balance sheet at their estimated fair value. At the end of each reporting period, the change in estimated fair value during the period is recorded in other income (expense), net in the statement of operations and comprehensive loss. We estimated the fair values of these warrants using the market approach based on the proximity of the valuation date to the closing of an additional Series B financing in December 2012. For each period subsequent to December 2012, we estimated the fair value of the warrant liability by applying a probability of two exit scenarios, going public or remaining private. In all instances, we utilized an OPM to allocate the value of the company to the warrants. We will continue to adjust the carrying value of the warrants until such time as these instruments are exercised, expire or convert into warrants to purchase shares of our common stock. At that time, the liabilities will be reclassified to additional paid-in-capital, a component of stockholders' deficit. The closing of this initial public offering will result in this reclassification.

JOBS Act Accounting Election

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Recent Issued and Adopted Accounting Pronouncements

In June 2014, the FASB issued ASU No. 2014-12, *Compensation – Stock Compensation or Topic 718: Accounting for Share-Based Payments When the Terms of an Award Provide That a Performance Target Could be Achieved After a Requisite Service Period*, or ASU 2014-12. Companies commonly issue share-based payment awards that require a specific performance target to be achieved in order for employees to become eligible to vest in the awards. ASU 2014-12 requires that a performance target that affects vesting and that could be achieved after the requisite service period should be treated as a performance condition. The performance target should not be reflected in estimating the grant date fair value of the award. Compensation cost should be recognized in the period in which it becomes probable that the performance target will be achieved. ASU 2014-12 will be effective for our fiscal years beginning fiscal 2016 and interim reporting periods within that year, using either the retrospective or prospective transition method. Early adoption is permitted. We are currently evaluating the effect of the adoption of this guidance on the financial statements.

In June 2014, the FASB issued ASU No. 2014-10, *Development Stage Entities Topic 915: Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation*, or ASU 2014-10. ASU 2014-10 removes all incremental financial reporting requirements regarding development-stage entities, including the removal of Topic 915 from the FASB Accounting Standards Codification. In addition, ASU 2014-10 adds an example disclosure in Risks and Uncertainties (Topic 275) to illustrate one way that an entity that has not begun planned operations could provide information about risks and uncertainties related to the company's current activities. ASU 2014-10 also removes an exception provided to development-stage entities in Consolidations (Topic 810) for determining whether an entity is a variable interest entity. ASU 2014-10 will be effective for our fiscal years beginning 2016 and interim

reporting period beginning in fiscal 2016. The revisions to Consolidation (Topic 810) are effective for our fiscal years beginning fiscal 2016. Early adoption is permitted. We have elected to early adopt this guidance as it relates to all incremental financial reporting requirements regarding development-stage entities.

In May 2014, the FASB issued ASU No. 2014-09, or ASU 2014-09, *Revenue from Contracts with Customers* (topic 606), or ASU 2014-09. ASU 2014-09 requires entities to recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. ASU 2014-09 requires entities to disclose both qualitative and quantitative information that enables users of financial statements to understand the nature, amount, timing and uncertainty of revenue and cash flows arising from contracts with customers, including disclosure of significant judgments affecting the recognition of revenue. ASU 2014-09 will be effective for our fiscal years beginning 2017 and interim reporting periods within that year, using either the retrospective or cumulative effect transition method. Early adoption is not permitted. We are currently evaluating the effect of the adoption of this guidance on the financial statements.

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern*, or ASU 2014-15. ASU 2014-15 requires management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date the financial statements are issued and provides guidance on determining when and how to disclose going concern uncertainties in the financial statements. Certain disclosures will be required if conditions give rise to substantial doubt about an entity's ability to continue as a going concern. ASU 2014-15 applies to all entities and is effective for annual and interim reporting periods ending after December 15, 2016, with early adoption permitted. We do not expect that the adoption of this guidance will have a material effect on the financial statements.

In November 2014, the FASB issued ASU No. 2014-16, *Derivatives and Hedging (Topic 815): Determining Whether the Host Contract in a Hybrid Financial Instrument Issued in the Form of a Share is More Akin to Debt or to Equity*, or ASU 2014-16. ASU 2014-16 was issued to clarify how current U.S. generally accepted accounting principles should be interpreted in evaluating the economic characteristics and risk of a host contract in a hybrid financial instrument that is issued in the form of a share. In addition, ASU 2014-16 was issued to clarify that in evaluating the nature of a host contract, an entity should assess the substance of the relevant terms and features (that is, the relative strength of the debt-like or equity-like terms and features given the facts and circumstances) when considering how to weight those terms and features. The effects of initially adopting ASU 2014-16 should be applied on a modified retrospective basis to existing hybrid financial instruments issued in a form of a share as of the beginning of the fiscal year for which the amendments are effective. Retrospective application is permitted to all relevant prior periods. ASU 2014-16 is effective fiscal years, and interim periods within those fiscal years, beginning after December 15, 2015. Early adoption in an interim period is permitted. We are currently evaluating the impact of the adoption of ASU 2014-16 on the financial statements.

Quantitative and Qualitative Disclosure about Market Risk

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10.0% change in interest rates would not have a material effect on the fair market value of our portfolio. Accordingly, we would not expect our operating results or cash flows to be affected to any significant degree by a sudden change in market interest rates on our investment portfolio.

We do not believe that our cash and cash equivalents have significant risk of default or illiquidity. While we believe our cash and cash equivalents and certificates of deposit do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash and cash equivalents at a financial institution that are in excess of federally insured limits.

Business

Overview

We are a clinical-stage specialty pharmaceutical company focused on the development and commercialization of novel and proprietary combination therapies that address significant unmet medical needs. Our initial focus is on the development of Hydros-TA, our proprietary, potentially best-in-class intra-articular, or IA, injectable product candidate to treat pain associated with osteoarthritis, or OA, of the knee. Current joint injection, or intra-articular, treatments for OA pain include corticosteroids, commonly known as steroids, which provide short-term relief, and viscosupplements, which provide pain relief over the longer-term. In contrast, Hydros-TA utilizes our proprietary cross-linking technology to deliver both rapid pain relief with a low dose steroid triamcinolone acetonide, or TA, and sustained pain relief with our proprietary hyaluronic acid viscosupplement. In our Phase 2b study of 98 patients, though not designed to show statistical significance, Hydros-TA demonstrated better pain reduction at all time points measured than Synvisc-One, the U.S. market-leading viscosupplement. We are currently studying Hydros-TA in an international Phase 3 trial enrolling up to 510 patients (of which approximately 350 patients have been enrolled as of March 31, 2015), and we expect to open an investigational new drug application, or IND, and begin to enroll U.S. patients in our second Phase 3 trial in mid-2015.

OA is a joint disorder involving the degradation of the IA cartilage, joint lining, ligaments and, ultimately, underlying bone. OA results in inflammation of the soft tissue and bony structures of the joint, which worsens over time and leads to progressive thinning of articular cartilage. Symptoms of this disease include pain, stiffness, swelling and limitation in the function of the joint. There is no known way to reverse the progression of OA and while there are a number of therapeutic options to treat the pain associated with OA, even with treatment, the disease typically continues to progress and patients may eventually require joint replacement surgery, often referred to as total knee arthroplasty, or TKA. Relative to therapeutic options to treat the pain, TKA is very expensive, with a cost of approximately $33,000 to $40,000 for an initial surgery and $74,000 for a revision surgery, thereby resulting in a meaningful burden on the healthcare system.

OA severity is generally graded on a scale from one to four. When OA advances and oral or topical drug treatments are not sufficient to effectively address the associated pain, physicians often turn to IA treatments, such as steroids, and hyaluronic acid, or HA, viscosupplements. While steroid injections can provide rapid pain relief, they generally provide only short-term pain relief of two to four weeks post injection. On the other hand, while HA injections can often provide long-term pain relief of up to approximately six months, they do not generally begin to provide peak pain relief until five weeks post injection. As a result, we believe there is a significant unmet medical need for a single product that provides both rapid and sustained pain relief in a safe and effective manner.

In the United States, there are over 27 million patients with OA, and approximately half of all adult patients will develop symptomatic OA of the knee during their lifetime. According to Millennium Research Group, in 2012, 1.65 million IA knee injections of hyaluronic acid, or HA, were administered. In the same year, worldwide sales of HA were approximately $1.76 billion, $726 million of which came from the United States. Millenium Research Group estimates that sales of HA will grow at a compound annual growth rate of approximately 8.9% in the United States to reach approximately $1.1 billion in 2017, and that worldwide sales of HA will reach approximately $2.4 billion in 2017.

We have formulated our Hydros-TA combination product with the goal of achieving both rapid pain relief through a low dose steroid component, and sustained pain relief of up to six months with Hydros, our proprietary HA. Hydros-TA has exhibited rapid and sustained relief of OA pain in our clinical trials to date. We believe the use of a low dose steroid, which is approximately one quarter the dosage of a common clinically-injected dose, will safely provide the rapid pain relief currently missing from commercially-available viscosupplements. We believe that if Hydros-TA can demonstrate sustained, safe and effective pain relief for advanced OA patients over a two week to six month timeframe, it also may delay time to TKA, which would confer significantly meaningful benefits to these patients and provide a strong pharmacoeconomic argument to payors.

In COR1.0, our completed multi-center, randomized, double-blind, three-arm Phase 2b study of 98 patients with grade two and grade three OA of the knee, we studied the use of Hydros-TA against Hydros alone (absent TA) and against Synvisc-One, the U.S. market-leading viscosupplement. Though we did not design COR1.0 to enroll a sufficient number of patients in the study to demonstrate statistical significance generally, Hydros-TA demonstrated better pain reduction than Synvisc-One at all-time points measured (2, 6, 13 and 26 weeks), with fewer product-related adverse events reported than Synvisc-One. We believe that the results of our Phase 2b study suggest that Hydros-TA could become a best-in-class first line injectable treatment of choice for OA pain management compared to existing therapies, by providing safe, effective, rapid and sustained pain relief.

We engaged in two formal meetings with the FDA in December 2011 and April 2014 regarding Hydros-TA's clinical development program. We are currently studying Hydros-TA in our COR1.1 trial, a Phase 3, multi-center, international, randomized, double-blind, three-arm trial enrolling up to 510 patients (of which approximately 350 patients have been enrolled as of March 31, 2015) with grade two and grade three OA of the knee, comparing treatment with Hydros-TA to treatment with Hydros and with TA, on a standalone basis. We expect to begin U.S. patient enrollment in our second Phase 3 trial, COR1.2, in mid-2015. Since TA is an approved product in different pharmaceutical preparations, we will rely on the FDA's prior findings of safety and efficacy for TA, and thus, the Hydros-TA new drug application, or NDA, will benefit from being filed under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or the FDCA, by eliminating some of the pre-clinical safety studies. TA is an approved drug and we have confirmed with the FDA that we can utilize the FDCA Section 505(b)(2) process and rely on existing safety data for the TA drug product. Hydros is considered a new molecular entity, or NME, and full pre-clinical testing is required and underway. However, since Hydros-TA is our product candidate, not Hydros alone, in order to obtain regulatory approval of Hydros-TA, Hydros will not have to undergo any clinical testing independent of the Hydros-TA studies. We are required to complete two Phase 3 clinical trials and one safety trial in order to satisfy the requirements for the demonstration of safety and efficacy of Hydros-TA in our initial indication for OA pain in the knee.

Following NDA approval, we expect to commercialize Hydros-TA using a small, 50 to 100 person specialty sales force targeting orthopedic surgeons, rheumatologists and pain specialists, the primary prescribers of IA steroids and viscosupplements. Physicians and payors are very familiar with the product category and use both HA and TA injectable products. If we are able to demonstrate that Hydros-TA provides rapid and sustained pain relief over a six month period, we believe that Hydros-TA will be well-positioned to become a leader in the OA IA injectable market. We own the global development and commercialization rights to Hydros-TA, except in China, Taiwan, Hong Kong and Macau, and would plan to commercialize Hydros-TA ourselves in the United States and through partners in the rest of the world. We have two issued U.S. patents and seven issued non-U.S. patents, the earliest of which will expire in 2030, and 18 patent applications worldwide covering our Hydros platform technology, including claims directed to composition of matter, methods of use and product-by-process.

Our executive management team has held senior positions at leading biopharmaceutical and medical technology companies and possesses substantial experience across the spectrum of drug discovery, development and commercialization. Our chief executive officer was previously the CEO of NeoMend, a leading developer and supplier of sprayable surgical sealants and anti-adhesion products, which was sold to C. R. Bard in 2012. Other members of our senior management team have also played key roles at Baxter, Angiotech, Merck, ALZA Corporation and other biopharmaceutical and medical technology companies in successfully developing and commercializing therapeutics.

Our Strategy

We intend to develop and commercialize novel and proprietary combination therapies for patients with osteoarthritis. The core principles of our strategy are to:

- ***Successfully complete our Phase 3 clinical trials for Hydros-TA and obtain FDA approval to market Hydros-TA.*** We are actively enrolling patients internationally in COR1.1, our first Phase 3 clinical trial of

Hydros-TA for the treatment of OA pain in the knee. During meetings with the FDA, we addressed elements of our development plan for Hydros-TA and the FDA indicated that COR1.1 appears adequately designed to constitute a Phase 3 trial. We expect to initiate COR1.2, our second Phase 3 trial, to open an IND and begin to enroll U.S. patients in COR1.2 in mid-2015, and to report primary endpoint results from COR1.1 in early 2016 and COR1.2 by the end of 2016. We anticipate submitting our NDA for Hydros-TA in early 2017.

- ***Expand our Hydros-TA therapy to treat OA pain in additional joints.*** We believe Hydros-TA is a platform therapy for treating OA pain in multiple joints in the body. While our initial focus is on OA pain in the knee, we intend to use a portion of the proceeds of this offering to accelerate our development of Hydros-TA for the treatment of OA pain in the hip, shoulder, ankle, spine and other joints in the body. We do not believe that Hydros-TA will require reformulation to be used in additional joints affected by OA.

- ***Build commercial capabilities in the United States and selectively partner outside of the United States to maximize the value of Hydros-TA.*** We intend to commercialize Hydros-TA, if approved, in the United States through our own focused sales force of approximately 50 to 100 sales people, which we will build in connection with U.S. approval of Hydros-TA. We have partnered commercial rights for Hydros-TA in China, Taiwan, Hong Kong and Macau to Shanghai Jingfeng Pharmaceuticals Co., Ltd., or Jingfeng. In other international markets, we intend to partner with established pharmaceutical companies to maximize the value of Hydros-TA without the substantial investment required to develop independent sales forces in those geographies.

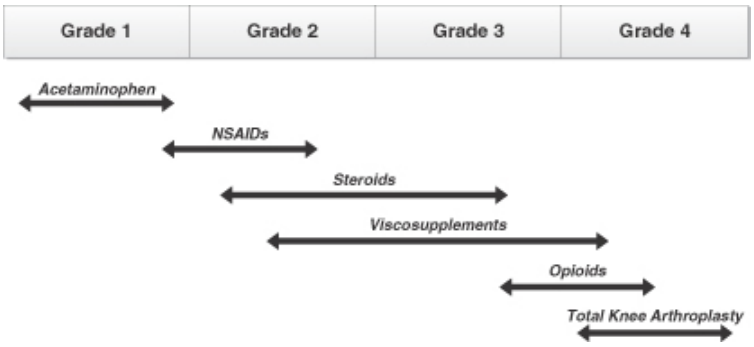
- ***Utilize our strong management team's expertise to develop and commercialize Hydros-TA and other novel combination products.*** Our management team has extensive experience in designing and implementing efficient and effective drug development programs, and in building sales forces and bringing new therapies to market. We intend to maintain an organizational structure designed to allow us to cost-effectively advance our development and commercialization plans.

Osteoarthritis

Osteoarthritis, or OA, is a progressive, degenerative joint disorder involving the degradation of the IA cartilage, joint lining, ligaments and underlying bone. OA results in inflammation of the soft tissue and bony structures of the joint, which worsens over time and leads to progressive thinning of articular cartilage. Symptoms of this disease include pain, stiffness, swelling and limitation in the function of the joint. There is no known way to reverse the progression of OA and while there are a number of therapeutic options to treat the pain associated with OA, the disease typically continues to advance.

According to data from the Medical Expenditures Panel Survey, in 2007 OA accounted for medical care expenditures of approximately $185.5 billion. The National Arthritis Data Workgroup reported that 27 million Americans over the age of 18 with OA. According to the Centers for Disease Control and Prevention, this number is likely to increase to 67 million Americans by 2030. While there are many potential risk factors that may increase the likelihood of an OA diagnosis, obesity, sports injuries and excessive mechanical stress are among the top contributing factors.

Beyond diet, exercise and physical therapy, the early treatment options for OA range from limiting weight impact on the joints, to oral analgesics and non-steroidal anti-inflammatory drugs, or NSAIDs, such as aspirin and ibuprofen. When OA advances and oral or topical drug treatments are not sufficient to effectively address the associated pain, physicians often turn to IA treatments, such as steroids and HA viscosupplements. These IA therapies provide more localized and targeted pain relief to the affected joint. Finally, for patients who progress to end-stage OA, physicians will prescribe opioids which are highly addictive and tend to have numerous systemic side effects such as respiratory depression and constipation in older OA patients. The following graph sets out what we believe to be the standard treatment progression for the treatment of OA pain in the knee:



Steroids and Viscosupplements

Dosages of steroids ranging from 10 to 40 mg have been demonstrated to be safe and effective for IA injection. Steroids have a rapid onset of pain relief but the effect is short-term, generally lasting only two to four weeks post injection. A 2006 publication on IA steroids in the Cochrane Database of Systematic Reviews, which included 28 trials and 1,973 participants, concluded that IA steroids were effective for two to four weeks post injection, but that there was a lack of evidence to support effect on pain and function beyond that time frame. Furthermore, it is believed that steroids may cause articular cartilage damage, especially with higher doses and repetitive use. Guidelines for steroids usually include a warning against frequent use and recommend that they only be administered three to four times per year.

Viscosupplementation therapies include HA, which is a naturally occurring constituent of the extracellular matrix of body tissues and is found in the synovial fluid and articular cartilage of joints. HA functions as a lubricant for joints and aids in joint mobility. For people with osteoarthritis, however, the hyaluronic acid in their synovial fluid breaks down and leads to joint pain and stiffness. According to the European League Against Rheumatism, there is evidence to support the efficacy of HA-based viscosupplements in knee OA for pain reduction and function improvement. Studies have shown that HA injections can often provide pain relief of up to approximately six months. While viscosupplementation can provide OA pain relief for a longer duration than IA steroids, it typically has a delayed onset of pain relief and does not generally begin to provide peak pain relief until five weeks post injection. A 2006 Cochrane publication on viscosupplementation involving 76 randomized, controlled trials confirmed that viscosupplements did not begin to provide peak pain relief until five weeks post injection. According to Millennium Research Group, the global market in 2012 for HA viscosupplementation was valued at approximately $1.76 billion, the current global market is estimated at over $2 billion and the global market in 2017 is estimated at approximately $2.4 billion.

The global OA pain therapeutics market was estimated to be $4.5 billion in 2011 and is expected to grow to over $6.1 billion by 2019, according to a report from GlobalData. According to Millennium Research Group, in 2012, 1.65 million IA knee injections of HA were given. In the same year, worldwide sales of HA were approximately $1.76 billion, $726 million of which came from the United States.

Total Knee Arthroplasty: Despite the use of currently available treatments, many OA patients experience persistent and worsening pain. Patients and their doctors therefore ultimately opt for TKA, which is generally the last option for the treatment of OA. Compared to other treatments, this invasive surgery is an expensive option, with an initial surgical procedure cost of approximately $33,000 to $40,000. Available data suggest that approximately 600,000 TKA procedures are performed annually in the United States at a cost of $9 billion per year in aggregate. Because patients are receiving TKAs more frequently and at a younger age, surgery to replace a previously performed TKA, known as revision surgery, is increasingly common and the average cost of a revision is approximately $74,000. Revision surgeries are not only more costly, they are also associated with significantly higher morbidity and failure rates than the initial TKA surgery. Because of these factors, TKAs are not ideal for younger patients that are likely to outlive the useful life of their implant, which is typically 15 to 20 years.

Due to the expense of surgery and the limitations of treatments administered to prevent such surgeries, there exists a need for an alternative treatment that could provide both rapid and sustained relief from OA pain and potentially delay the need for joint replacement surgery.

Our Solution — Hydros-TA

Hydros-TA is a combination IA product, designed to provide both rapid and sustained pain relief with a single 6 ml intra-anticular injection, comprised of 52 mg of bacterially derived HA and 10 mg of TA. Rapid relief is provided from our low dose steroid component and sustained pain relief, up to six months, is provided from our proprietary HA component. Hydros-TA is comprised of bacterially derived HA-based hydrogel particles suspended in a solution of hyaluronic acid. The hydrogel particles contain the steroid, triamcinolone acetonide, which is entrapped within these particles. The dose of TA used in Hydros-TA is 10 mg, which is one quarter of the dose of TA that is often administered clinically for IA injections into the knee. We believe the incorporation of a low dose steroid into Hydros-TA provides a means of rapid pain relief currently missing from commercially-available HA products.

We have developed a proprietary methodology to cross-link hyaluronic acid in order to form our novel hydrogels. The chemistry used to cross-link the hyaluronic acid does not produce harmful reaction by-products that would otherwise need to be removed from the hydrogel during the manufacturing process. This enables the direct incorporation of biologically-active agents into the hydrogel without the requirement for further purification. By incorporating the steroid component of Hydros-TA directly into the hydrogel, the effective particle size of the steroid is dramatically increased. The large-sized hydrogel particles are not readily cleared from the joint immediately following IA injection, which may allow for better retention in the joint and better protection of the cartilage surface from direct exposure to the steroid crystals. In addition, Hydros-TA is comprised of both a soluble HA component and a cross-linked HA hydrogel component. Clinical studies have shown that soluble HA provides pain relief from OA knee pain, while HA hydrogels are known to be retained in the joint for a longer duration of effect than soluble HA. By utilizing these two forms of HA, we have designed Hydros-TA to combine the proven pain-relieving benefits of soluble HA with the duration benefits of HA hydrogel. Moreover, we believe that the molecular weight of our soluble HA component, at 700-1,000 kDa, is optimized for pain relief and that our HA hydrogel component, with approximately 2.5 times more HA hydrogel than Synvisc-One, is optimized for duration of effect. Additionally, we designed our Hydros platform from a bacterially derived HA, without the presence of animal proteins common in other viscosupplements, which eliminates a source of a potential adverse immune response. We believe that a clinically-proven and FDA-approved combination Hydros-TA product will provide a compelling alternative to performing sequential injections of steroids and viscosupplements. Additionally, the ready-to-use single injection format means that there is no product manipulation required before use. From the physician’s standpoint, this means that the product is easy to use and, because every joint injection poses a risk of infection, may reduce the likelihood of potential joint infections when compared to a procedure that involves separate injections of a steroid and a viscosupplement. We believe that the versatility provided by our proprietary cross-linking combination will enable Hydros-TA to potentially address current shortcomings in the OA pain relief treatment spectrum for the knee, as well as provide both rapid and sustained relief for other joints affected by OA pain, such as hip, shoulder, spine and ankle joints.

Hydros-TA Clinical Program

Hydros-TA is a drug/device combination product regulated through the FDA's Center for Drug Evaluation and Research, or CDER. We do not currently have an open IND, so we have designed and implemented our Phase 3 program in close communication with the FDA. The chemistry, manufacturing, control and development for Hydros-TA have, in principle, been outlined and expectations communicated by the FDA to enable an IND to be opened in mid-2015. Our COR1.1 Phase 3 study protocol, including primary and secondary endpoints and statistical analysis plan, was developed in conjunction with formal pre-IND meetings with the FDA in which our COR1.0 Phase 2b study data was presented. In these meetings, we also addressed the study protocol for our second Phase 3 study, COR1.2, which will be designed as a two arm, TA-controlled study. The FDA also clarified the requirement for the number of patients required for the safety database and indicated that we could utilize an open-label safety trial to collect these data. We expect to initiate COR1.2, our second Phase 3 trial, to begin enrolling U.S. patients in COR1.2 in mid-2015, and to report primary endpoint results from COR1.1 in early 2016 and COR1.2 by the end of 2016.

Clinical Design and Statistical Analysis: As is typical for osteoarthritis clinical studies, our studies are designed using the Western Ontario and McMaster Universities Osteoarthritis Index, or WOMAC. The WOMAC is a validated and accepted instrument developed to assess and quantify pain, joint stiffness and disability related to osteoarthritis of the knee and hip. The WOMAC contains 24 questions, five related to pain, two to stiffness and 17 to physical function. It can be used to monitor the course of the disease or to determine the effectiveness of a variety of interventions. These measurements are obtained both prior to IA injection, referred to as a baseline measurement, and then following injection, at several post-treatment visits. In the Hydros-TA clinical studies, the primary measure of effectiveness is assessed based on the differences between treatment groups in changes from baseline to post-treatment visits in the WOMAC pain scale. The secondary outcome measurement includes changes from baseline in WOMAC stiffness and WOMAC function. The differences between treatment groups can be assessed using a statistical technique called a repeated measures analysis of covariance, referred to as ANCOVA, which estimates treatment effects where there are repeated assessments of a measurement captured over time. Using repeated measures, the ANCOVA model provides the ability to assess the treatment effect in the presence of other explanatory variables, or covariates, such as the baseline value or the study center at which the subject is enrolled.

Our studies also utilize the OMERACT-OARSI criteria to define the number and percentage of OMERACT-OARSI-defined positive "strict responders" (>50% and >20 mm improvements in WOMAC pain or function scores over baseline) in our clinical studies. This is an important measure of the consistency of the response seen across all subjects within a treatment group. Traditionally, viscosupplements provide responder rates of approximately 50%. The Cochran-Mantel Haenszel General Association statistic, stratified by study center, was used to assess differences among treatments and to assess differences in the pairwise comparisons between treatments in the OMERACT-OARSI response rate.

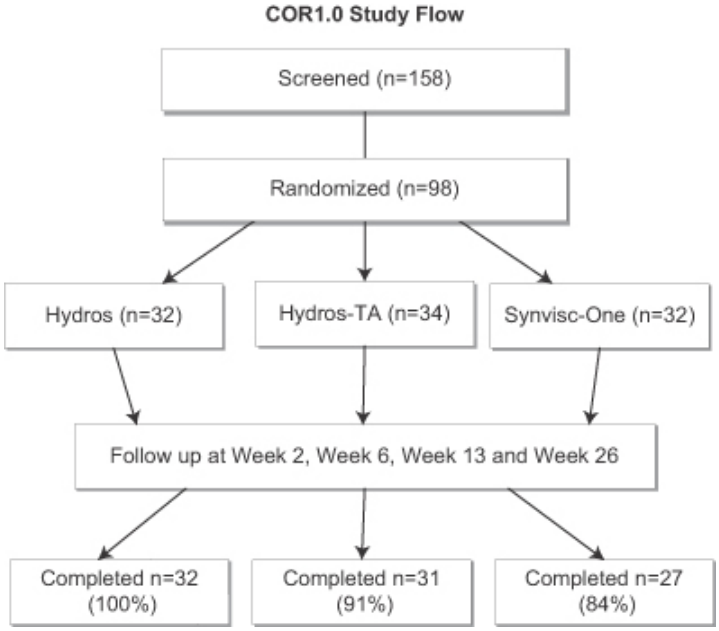
In the discussion below, statistical significance is denoted by p-values. The p-value is the probability that the reported result was achieved purely by chance (for example, a p-value <0.001 means that there is a less than a 0.1% chance that the observed change was purely due to chance). Generally, a p-value less than 0.05 is considered to be statistically significant. Certain trial results discussed below were evaluated using an analysis method referred to as "least square means." Least square means is a mean estimated from a linear model and is adjusted for other variables that may affect the experimental value.

COR1.0- Phase 2b Clinical Trial

Our Phase 2b clinical trial of Hydros-TA, known as COR1.0, was a prospective, multicenter, randomized, double-blind feasibility study to evaluate the safety and performance of Hydros-TA in subjects with OA of the knee. Eight clinical centers in Canada, Europe and the Caribbean participated in the COR1.0 trial. A total of 158 subjects were screened, 60 of whom were removed from the study for failure to meet the study protocol requirements. The most common reasons for subject removal from the study after screening included: pain scores too low in the treatment knee, pain scores too high in the non-treatment knee, a body mass index over 35, and previous treatment with pain-reducing therapies within the excluded pre-treatment timeframe. A total of 98 subjects were enrolled, treated and followed for six months post-treatment. Subjects were randomized 1:1:1 to three study treatment arms: Hydros-TA, Hydros (the viscosupplement without steroid) and Synvisc-One (the U.S. market leading HA viscosupplement).

All randomized subjects received one 6 mL IA injection in the treatment knee by an unblinded injecting physician. The treatment knee was the knee that met the inclusion criteria on WOMAC pain score and received one of the three IA injection treatments, as determined by sequential randomization at each study site. Subjects were seen by a treatment-blinded evaluating physician for post-treatment follow-up at two weeks, six weeks, 13 weeks and 26 weeks. Subjective symptom rating and physical assessment including a full WOMAC questionnaire were obtained at screening and each follow-up visit. Subject global assessment was obtained at 13 weeks and subject and physician global assessments were obtained at 26 weeks. Care was taken to maintain subject blinding at all times. Adverse events, or AEs, were solicited at all visits. Assessments of all AEs for all study visits were performed by a blinded physician. Any AE reported post-treatment was considered a treatment-emergent adverse event and was summarized by treatment group and assessed for relation to treatment and procedure. Eight subjects who were enrolled in the study did not complete the study for various reasons, including recommendation from the principal investigator physician that the subject needed additional medical treatment that would disqualify the subject from participation in the study, as well as persistent or worsening pain in the treatment knee leading to a subject's voluntary withdrawal from the study.

The below table illustrates the clinical train design of our COR1.0 Phase 2b study:



With a sample size of 98 subjects (32-34 subjects per group), COR1.0 was intended to provide preliminary information on the safety and tolerability of Hydros and Hydros-TA, as well as a preliminary review of efficacy of these two modalities as compared to the control, Synvisc-One, and to inform the design and powering of our Phase 3 trial. Intent-to-Treat, or ITT, methodology was used to analyze subjects by treatment group for efficacy and safety. The following table illustrates that COR1.0 treatment arms were well-balanced with respect to demographic and baseline characteristics, with balanced weighting of the baseline demographics of study subjects across treatment modalities including age, BMI, disease severity and pain levels in both treated and non-treated knees and duration of OA symptoms:

Category	Hydros n=32	Hydros-TA n=34	Synvisc-One n=32
Mean (SD) Age	59 (12)	61 (11)	59 (12)
Gender (N %)			
Male	12 (38%)	14 (41%)	16 (50%)
Female	20 (63%)	20 (59%)	16 (50%)
Mean (SD) Body Mass Index	29.8 (4.1)	29.0 (4.1)	29.0 (3.8)
Kellgren-Lawrence Grade for Treatment Knee (N %)			
Grade 2	18 (56%)	22 (65%)	18 (56%)
Grade 3	14 (44%)	12 (35%)	14 (44%)
Mean (SD) Pre-Treatment Average WOMAC score (mm)			
Treatment Knee	68 (9)	69 (11)	66 (12)
Non-treatment Knee	13 (8)	12 (9)	12 (8)
Mean (SD) Duration of Symptoms — Pre-Treatment in Treatment Knee (months)	64 (59)	74 (80)	69 (56)

The following table represents the baseline scores for each of the treatment groups, as well as the WOMAC pain score least square mean reductions from baseline over the full 26 week evaluation period, as well as at the 2, 6, 13 and 26 week time points post injection. The model estimated difference between the treatment groups is also represented.

Time Point	Hydros n=32	Hydros-TA n=34	Synvisc-One n=32	Extra Pain Reduction Hydros vs. Synvisc-One	Extra Pain Reduction Hydros-TAvs. Hydros	Extra Pain Reduction Hydros-TA vs. Synvisc-One
Baseline	68.1	69.4	66.4	N/A	N/A	N/A
2 weeks	-23.3	-35.6	-28.5	5.2	-12.4*	-7.2
6 weeks	-32.4	-33.4	-25.6	-6.7	-1.1	-7.8
13 weeks	-33.9	-33.3	-29.0	-4.9	0.6	-4.3
26 weeks	-32.4	-35.2	-28.9	-3.5	-2.8	-6.3
Overall	**-30.5**	**-34.4**	**-28.0**	**-2.5**	**-3.9**	**-6.4**

* Statistically significant.

Primary Endpoint: WOMAC pain score: Pain reduction from baseline was observed in all treatment groups, however, in general, Hydros-TA provided greater pain reduction compared to Synvisc-One at all study time points, as well as over the full study follow-up period of 26 weeks. As the above table illustrates, for the WOMAC pain score change from baseline, the least square mean reductions from baseline over 26 weeks, overall least-square means and standard errors (SE) were as follows: 30.5 (5.1) mm for Hydros, 34.4 (4.7) mm for Hydros-TA, and 28.0 (5.4) mm for Synvisc-One. Overall, the Hydros-TA estimated mean reduction represents an observed improvement over Synvisc-One of 6.4 mm ($p = 0.24$). Though we did not design our COR1.0 trial to enroll a sufficient number of patients to demonstrate statistical significance, generally this separation from Synvisc-One represented approximately 10% of the baseline score, a numerical amount generally considered “clinically meaningful” and, we believe, not often seen in viscosupplementation trials with active comparators.

Secondary Endpoints: The trend seen with our primary endpoint toward improved outcomes with Hydros-TA compared to Synvisc-One was consistent with our secondary endpoints of WOMAC stiffness, WOMAC function and responder analysis.

- *WOMAC stiffness score:* The least square mean changes in WOMAC stiffness score from baseline for the ITT population for each treatment group are 24.5 (5.8) mm for Hydros, 29.8 (5.3) mm for Hydros-TA, and 25.1 (6.1) mm for Synvisc-One. This represented an estimated difference of 4.7mm in stiffness scores for Hydros-TA compared to Synvisc-One.

- *WOMAC function score:* Hydros, Hydros-TA and Synvisc-One had reductions of 27.3 (5.4) mm, 30.0 (4.9) mm and 24.3 (5.6) mm, respectively, for the changes from baseline of the overall mean WOMAC function score. This represented a numerical improvement of 5.6 mm in function scores for Hydros-TA compared to Synvisc-One.

- *Strict OMERACT-OARSI responder analysis:* The percentages of strict OMERACT-OARSI responders for the Hydros and Hydros-TA groups were numerically higher than the strict responders for Synvisc-One group at both 13 and 26 weeks. At 13 weeks, the response rate for Hydros-TA was 71%, for Hydros 66% and for Synvisc-One 53%. At 26 weeks, the response rates were 59%, 65% and 69% for Synvisc-One, Hydros-TA and Hydros, respectively.

In our comparison of the pain reduction provided by Hydros-TA versus Hydros, we demonstrated the early onset of pain relief provided by the study product containing steroid (Hydros-TA) compared with the identical study product without steroid (Hydros). While there was not a statistically significant difference between Hydros-TA and Hydros over 26 weeks, there was a statistically significant 12.4 mm improvement in pain scores at the two-week time point for Hydros-TA versus Hydros (p=0.04). This result confirms the earlier onset of pain relief for Hydros-TA, the steroid containing therapy, versus Hydros alone, the non-steroid containing therapy. As illustrated in the table below, similar trends were seen for stiffness and function when Hydros-TA was compared to Hydros at two weeks post injection:

Time Point	Hydros n=32	Hydros-TA n=34	Difference	p-value
	Mean reduction (pain) from baseline [LSMeans (SE)]		Estimated between group difference	
Pain (WOMAC A)	-23.3 (5.6)	-35.6 (5.2)	-12.4	0.04
Stiffness (WOMAC B)	-18.4 (6.4)	-33.7 (6.0)	-15.3	0.03
Function (WOMAC C)	-20.2 (5.8)	-32.1 (5.3)	-12.0	0.05

The two-week pain score comparison between Hydros-TA and Hydros is identical to the first co-primary endpoint in our COR1.1 trial.

Adverse events: Adverse events, or AEs, for 15 subjects were reported in COR1.0 as "Likely" or "Definitely" related to study treatment: six in the Synvisc-One group, six in the Hydros group and three in the Hydros-TA group. There were a total of 19 AEs related to study treatment in these 15 subjects: nine in the Synvisc-One group, seven in the Hydros group and three in the Hydros-TA group. The most commonly reported AEs related to study treatment were arthralgia and joint stiffness. These results are summarized in the following table:

AE Description	Synvisc-One n=32	Hydros-TA n=34
Arthralgia (non-inflammatory joint pain)	5	1
Joint Stiffness	2	0
Joint Swelling	1	0
Injection/Application Site Warmth	1	1
Injection Site Movement Impairment	0	0
Injection Site Pain	0	1
Total Product-Related AEs	**9**	**3**

A total of seven subjects reported Serious Adverse Events (SAEs). In the Hydros group, the three reported SAEs were colitis, broncho-pneumonia and arthralgia. In the Hydros-TA group, the two reported SAEs included a report of a meniscal lesion and a cyst aspiration. Lastly, the two SAEs reported in the Synvisc-One group were a meniscal lesion and an elective surgery. All SAEs were considered unlikely or definitely not related to treatment and had resolved by the termination of the study. Treatment emergent adverse events were reported in 69% of all subjects treated, the most common of which were arthralgia, joint swelling, joint stiffness, headache and back pain.

Key Observations from COR1.0: The results from COR1.0 suggest that a single injection of Hydros-TA was well-tolerated and could relieve pain associated with symptomatic OA of the knee over 26 weeks. Hydros-TA demonstrated a numerically higher pain relief at all time points after injection when compared with Synvisc-One. The percentage of subjects who responded favorably to the product as measured by the OMERACT-OARSI responder rate was higher in the Hydros and Hydros-TA groups when compared to Synvisc-One. The study endpoints showed strong trends toward an enhanced effect compared to Synvisc-One, although these trends did not reach statistical significance.

To our knowledge, this is the first clinical study to report on the safety and effectiveness of a single-injection viscosupplement that combines HA and corticosteroid for the treatment of knee OA. Reductions in WOMAC pain scores observed in this study suggest that this combination may have a faster onset of pain relief compared to non-steroid containing products and may provide improved pain relief over the full 26 weeks post injection. These results reflect a synergistic effect of combining HA with a corticosteroid.

Phase 3 Clinical Trial Program

COR1.1

The first of our two pivotal Phase 3 trials began enrollment in mid-January 2014. We are actively enrolling up to 510 subjects at approximately 30 sites in Australia, Canada, New Zealand, Europe and the Caribbean. As of March 31, 2015, approximately 350 subjects have been enrolled in COR1.1. Subjects with OA grade two and grade three are randomized equally between three treatment arms; Hydros-TA, Hydros and TA. The objective of the trial is to demonstrate the safety and efficacy of Hydros-TA and the contribution of each of the two components in the Hydros-TA therapy. Our inclusion and exclusion criteria are designed to reduce the potential for placebo effect and to screen out non-responders where possible. The primary comparisons measure changes in pain under the WOMAC pain scale of Hydros-TA versus Hydros at two weeks and Hydros-TA versus TA at 26 weeks. Secondary endpoints include WOMAC function changes, subject and physician global assessment and an OMERACT-OARSI responder rate. We expect top-line data from this trial by the end of 2015.

COR1.2

The second of our two Phase 3 trials is scheduled to begin in mid-2015. We plan to enroll approximately 340 subjects at 20 to 30 sites in the United States, Australia, Canada and Europe. Subjects with OA grade two and grade three will be randomized equally between two treatment arms; Hydros-TA and TA. The objective of the trial will be to demonstrate the superiority of Hydros-TA compared to TA at 26 weeks post injection by measuring the change from baseline on the WOMAC pain scale. Secondary endpoints will include changes in WOMAC function, subject and physician global assessment and an OMERACT-OARSI responder rate. We expect top-line data from this trial by the end of 2016.

COR1.3

In addition to the COR1.1 and COR1.2 trials required for approval, we will need to collect safety data from an additional 400 to 450 patients, which will provide us with approximately 800 patients to make up our safety database. This trial will be conducted as a non-randomized, non-blinded trial. Patients who are screen failures for the COR1.1 and COR1.2 trials may be candidates for inclusion in this open-label trial.

Additional Clinical Requirements

A small bioavailability study will be required to demonstrate that the circulating levels of triamcinolone acetonide are not higher after Hydros-TA treatment than what has been demonstrated with commercially approved triamcinolone acetonide formulations. Since products such as Kenalog (triamcinolone acetonide) are approved at 10 and 40 mg doses, and up to 40 mg is commonly injected in the knee joint, we believe that this trial is just confirmatory and constitutes minimal to no clinical risk. It is possible that a study may be required to show the absorption, distribution, metabolism and excretion profile of Hydros-TA. The FDA has indicated that if Hydros is undetectable in plasma using a sensitive bio-analytical assay, this study requirement may be waived. If the study is required, a total of twelve subjects should be adequate for the Hydros evaluation without radiolabeling. If radiolabeled, five or six subjects with adequate data should be sufficient.

Hydros-TA Pre-clinical Program

There are no validated pre-clinical animal models for OA that have been shown to directly translate into successful efficacy outcomes for viscosupplementation products. Thus, the approach that we undertook in developing the Hydros and Hydros-TA products, was to demonstrate safety and biocompatibility of the Hydros and Hydros-TA pre-clinically and then test these products in the clinical setting for the efficacy signal. We completed initial ISO 10993 biocompatibility testing as well as initial toxicity testing in a large animal model. The data generated from these pre-clinical studies were sufficient to initiate human clinical testing of the Hydros and Hydros-TA products in Canada and Europe.

Pre-clinical: Biocompatability Studies

Hydros	Result
Cytotoxicity: ISO MEM Elution Assay with L-929 Mouse Fibro-blast Cells	Non-cytotoxic
Intracutaneous Reactivity Test	Non-irritant
Guinea Pig Maximization Sensitization Test	Non-sensitizing
Acute Systemic Toxicity	Non toxic
Subcutaneous Implant Test — Two Week Duration	Non-Irritant compared to Synvisc-One
Genotoxicity — Bacterial Mutagenicity Test (Ames Assay)	Non-mutagenic
Genotoxicity — Mutagenicity: In Vitro Mouse Lymphoma Assay	Non-mutagenic
Genotoxicity — Mutagenicity: In Vivo Mouse Micronucleus Assay	Non-mutagenic
Subchronic toxicity — 4 week in Rats	Non toxic, slight-irritant compared to Saline

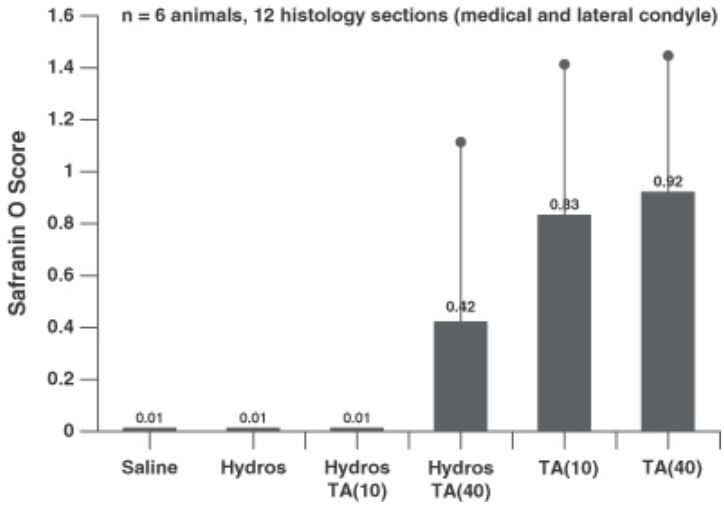
Hydros-TA	Result
Cytotoxicity: ISO MEM Elution Assay with L-929 Mouse Fibroblast Cells	Non-cytotoxic
Intracutaneous Reactivity Test	Non-irritant
Guinea Pig Maximization Sensitization Test (The Magnusson and Kligman method)	Non-sensitizing

Pre-clinical: Safety Studies

Study Number/ Species/Study Type	Result
REP-10008 Goat Safety Study (GLP) IA Injection with 28 day follow-up	No systemic or local toxicity
REP-10009 Goat Safety Study (GLP) IA Injection with 88 day follow-up	No systemic or local toxicity
REP-09014 Goat Safety Study (Non-GLP) IA Injection with 14 and 28 day follow-up	No systemic or local toxicity
REP-09015 Goat Safety Study (Non-GLP) 24 hour synovial fluid and joint evaluation	No local toxicity

A study in a goat model showed that the incorporation of the triamcinolone acetonide into the hydrogel component of Hydros-TA appeared to reduce the proteoglycan loss from the cartilage, as shown by changes in Safranin O staining of the cartilage, in comparison to injection of the triamcinolone acetonide alone. In this study the following formulations were injected into the stifle of a goat in volumes equivalent to 10 mg and 40 mg: saline, Hydros, Hydros-TA and TA. Treatment groups consisted of six goats per group with each goat receiving a single injection into the right stifle. After 28 days, the goats were sacrificed and the joints were analyzed histologically. Histological sections were taken from the lateral femoral condyle and the medial femoral condyle and these sections were stained with Safranin O. A loss in the intensity of the Safranin O staining indicates a loss of proteoglycans from the cartilage structure, which is indicative of changes in the health of the cartilage. The analysis of the Safranin O stained histological sections of the cartilage showed that for comparable doses of TA, incorporation of the TA into the hydrogel component of the Hydros-TA resulted in less proteoglycan loss from the cartilage. For Hydros-TA

that contained an equivalent of a 10 mg clinical dose, there was no loss in Safranin O staining observed, whereas there was a loss in Safranin O staining when a similar dose of TA that was not incorporated into the hydrogel that was administered. This indicates that incorporation of the steroid into the hydrogel component of the Hydros-TA is beneficial to the health of the cartilage as compared the steroid alone.



In October 2014, we received minutes from the FDA regarding the proposed pre-clinical program, consisting of safety studies required by the FDA that are standard for NMEs. We intend to complete these studies to ensure the FDA can assess the pre-clinical profile of Hydros-TA.

Research and Development

Our research and development efforts have focused on developing a proprietary versatile methodology to cross-link hyaluronic acid to form hydrogels. This methodology is versatile because slight alterations in the formula allow us to prepare hydrogels that can be pre-formed or prepared on site and can range in texture from soft to hard gels. The chemistry used to cross-link the hyaluronic acid does not produce harmful reaction by-products that must be removed from the hydrogel during the manufacturing process. This enables the direct incorporation of biologically-active agents into the hydrogel without the need for further purification. Thus, these prepared hydrogels can be used directly without further processing. Additionally, biologically-active agents such as small molecule drugs, certain proteins and cells can be incorporated into the hydrogel. Such hydrogel formulations can be applied topically or parenterally.

Hydros-TA — other joints. We have focused our product development efforts on developing Hydros-TA for the treatment of OA pain in the knee. As this program progresses along the path to regulatory approval in the United States, we may explore the potential use of Hydros-TA in treating pain in other joints affected by OA. Joints affected by OA include the finger, hip, shoulder, ankle and temporomandibular joints. The initial target for the next product development effort for OA may likely be the hip joint.

Hydros. We have focused our current development efforts on Hydros-TA. During the course of the current clinical program, we expect to generate clinical data for Hydros, our proprietary HA-based hydrogel. Hydros is identical to Hydros-TA, with the exception that it does not contain triamcinolone acetonide. Depending on the data that we obtain from the on-going clinical study, we may pursue regulatory approval of Hydros.

Commercial Strategy

According to the American Association of Orthopedic Surgeons, or AAOS, there are approximately 17,795 active orthopedic surgeons in the United States. According to the Association of American Medical Colleges, there are approximately 3,920 practicing rheumatologists in the United States. According to the American Society of Regional Anethesia and Pain Medicine, there are approximately 4,000 pain specialists in the United States. We believe we can effectively cover these specialties and successfully execute our future commercial plans using a cost-efficient strategy, particularly given that orthopedists, rheumatologists and pain specialists are familiar with IA injections.

We intend to build a commercial infrastructure in the United States to effectively support the marketing of Hydros-TA, if approved. We believe that we can cost-effectively penetrate the universe of prescribing orthopedic surgeons, rheumatologists, and pain specialists in the United States with a targeted, specialty sales force of approximately 50 to 100 representatives. Support for this team will include sales management, internal sales support, distribution support and an internal marketing group. Additional requisite capabilities will include focused management of key accounts such as managed care organizations, group purchasing organizations, government accounts and private insurers.

Outside of the United States, we have entered into a license agreement with Jingfeng for China, Taiwan, Hong Kong and Macau and are exploring selective partnerships with other third parties for the commercialization of our products.

Competition

Our industry is highly competitive and subject to rapid and significant technological change. The large size and expanding scope of the pain market makes it an attractive therapeutic area for biopharmaceutical businesses. Our potential competitors include pharmaceutical, biotechnology and specialty pharmaceutical companies. Several of these companies have robust drug pipelines, readily available capital and established research and development capacities. We believe our success will be driven by our ability to actively focus on OA patients and their needs.

The key competitive factors affecting the success of Hydros-TA, if approved, are likely to be efficacy, durability, safety, price and the availability of reimbursement from government and other third-party payors. We believe we will compete favorably by having a fast-acting, long lasting, effective candidate that has a validated mechanism of action for OA pain relief and an attractive safety profile.

Intra-articular Therapies. Currently available steroid injections are effective at providing pain relief within a couple of days, but they do not last for more than about a month and can have a damaging effect on the healthy cartilage. Most of these steroid injections are interchangeable with the choice usually stemming from cost to the patient and physician preference. Specifically, Flexion Therapeutics is developing FX006 which is a time release steroid composed of triamcinolone acetonide encapsulated in PGLA particles providing pain relief of up to approximately 10 weeks post injection. There are five multi-injection viscosupplements (Hyalgan, Orthovisc, Supartz, Synvisc and Euflexxa) and three single-injection products (Synvisc-One, Gel-One and Monovisc) that are currently on the market. Each of these products is derived from HA, which generally does not begin to provide peak pain relief until five weeks post injection.

Combination and Other Therapies. A combination of viscosupplementation and corticosteroid is also being evaluated by Anika Therapeutics. The Anika product, called Cingal, is a combination of hyaluronic acid (Monovisc) and triamcinolone hexacetonide (TH) providing pain relief of up to approximately 12 weeks post injection. This product was recently evaluated in a three arm trial comparing Monovisc and Cingal to placebo. To our knowledge, the study results have not yet been released to the public, and this is the first human trial with this

product. Ampio Therapeutics is developing an injectable treatment for OA knee pain called Ampion. Ampion is comprised of aspartyl-alanyl diketopiperazine, an endogenous immunomodulatory molecule derived from the N-terminus of human serum albumin. To our knowledge, Ampion is currently under evaluation in a Phase 3 trial.

Coverage and Reimbursement

Viscosupplemention has become an important treatment option for patients with osteoarthritis of the knee. A number of viscosupplementation products are currently approved by the FDA for marketing in the United States with indications for use in OA of the knee. Each has demonstrated a statistically significant reduction in pain and improvement in function. In the United States, third-party payors (such as Medicare, Medicaid, and commercial health plans) provide coverage to individuals for medically necessary services. The Medicare program covers certain individuals who are disabled or aged 65 or older, two groups with a comparatively higher incidence of OA. The Medicare program is increasingly used as a model for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Since no uniform policy of coverage and reimbursement for medical products exists among third-party payors, we may be required to provide economic, scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

AAOS issued a guideline in 2008 in which it found that the benefits of viscosupplementation were inconclusive and was unable to recommend for or against their use. In May 2013, AAOS issued a revised guideline on treatment of OA of the knee that stated “we cannot recommend using hyaluronic acid for patients with symptomatic osteoarthritis of the knee”. AAOS stated that its recommendation was strong and was based on high quality supporting evidence related to lack of efficacy, rather than potential harm. In developing its 2013 guidelines, AAOS considered a different and smaller group of studies than it had in 2008 and found statistically significant positive treatment effects with respect to pain, function and stiffness. However, in 2013, it went on to consider whether the improvements in pain and function were large enough to pass “minimum clinically important improvement” thresholds and the evidence it considered approached, but did not pass, these thresholds.

While some third-party payors continue to cover HA for the treatment of OA of the knee after the publication of the AAOS guidelines, a number of third-party payors, including Blue Cross Blue Shield, have reversed their coverage policies and no longer cover the use of HA for the treatment of OA of the knee. Several payors still continue to cover viscosupplementation for patients with OA of the knee and related pain that interferes with function after more conservative therapies have been attempted. The more conservative therapies that payors expect to precede viscosupplementation include NSAIDs and intra-articular injection of steroids. Evidence-based review by payors has generally found a lack of reliable evidence that any particular brand of viscosupplement is superior to others when used for medically necessary indications. As a result, some payors may disfavor new products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Many payors also limit repeat treatment to 6 month intervals.

Manufacturing

We have relied on contract manufacturing organizations, or CMOs, to manufacture both the active pharmaceutical ingredient and final drug product dosage form for Hydros-TA that has been used as clinical trial material. We have manufactured the two intermediate components used in the manufacture of the hydrogel for the initial clinical studies. These two components will be outsourced to CMOs for future clinical material and for commercial production. Our management team has extensive experience with the management of a virtual supply chain consisting of CMOs, contract packaging operations and third-party logistics providers. We currently anticipate continuing to use CMOs to manufacture clinical material for future clinical studies and for the initial commercial product.

The manufacture of sterile injectables is a complex and expensive process that is subject to a high degree of regulatory oversight. All of our CMOs are experienced commercial manufacturers and are qualified by us before we begin to work with them. The patented and proprietary Hydros chemistry involves mild processing conditions and routine unit operations. Extensive development work has been completed to optimize the operations for commercial manufacture. Hyaluronic acid and triamcinolone acetonide, the two key raw materials for Hydros-TA, are readily available from multiple sources commercially.

Intellectual Property

Technology License Agreement with Shanghai Jingfeng Pharmaceutical Co., Ltd.

In November 2012, we entered into a technology license agreement with Jingfeng, pursuant to which we granted Jingfeng the exclusive right and license to develop, manufacture and commercialize Hydros-TA, or any improvements or modifications of Hydros-TA, for human and veterinary uses in China, Taiwan, Hong Kong and Macau. In these countries, Jingfeng is responsible for the manufacture and supply of Hydros-TA, the management and funding of all development activities, regulatory submissions and regulatory approvals for Hydros-TA, and the commercialization of Hydros-TA. Jingfeng is restricted from developing, manufacturing, using, distributing, marketing, importing and selling Hydros-TA outside of the foregoing territories.

In consideration for the exclusive license, we received a non-refundable up-front payment of $2.0 million ($1.7 million net of Chinese withholding tax). In November 2013, we received a non-refundable milestone payment of $0.4 million (net of Chinese withholding tax) upon the successful production by Jingfeng of the first batch of Hydros-TA. We are also eligible to receive future milestone payments of up to $1.5 million and commercialization royalty payments of up to approximately $5.0 million (each excluding Chinese withholding tax), based on the achievement of certain regulatory and commercialization milestones, respectively.

Our agreement with Jingfeng will expire upon the later of the date of the expiration of the last licensed patent or the invalidation of the last licensed patent. We have the right to terminate the agreement immediately upon written notice to Jingfeng in the event Jingfeng violates any of several covenants related to compliance with applicable laws. Jingfeng may terminate the agreement upon written notice if Jingfeng decides to withdraw from the market licensed products in a given country in the licensed territory due to scientific, technical, regulatory and/or commercial reasons after the parties have discussed the situation in good faith. Either party may terminate the agreement upon written notice if as a result of Jingfeng's withdrawal of a licensed product (a) there is no licensed product being commercialized or developed by Jingfeng in China, (b) there is no licensed product being marketed or sold in China for a specified period of time after such withdrawal, and (c) despite the parties' good faith efforts, the parties agree that there are no commercially viable licensed products or prospective licensed products available for sale in the licensed territory. Either party may terminate the agreement upon bankruptcy or insolvency of the other party, and either party may terminate the agreement for any material breach by the other party that is not cured within a specified time period.

Patents and Patent Applications

We seek to protect our product candidates and our technology through a combination of patents, trade secrets, proprietary know-how, FDA exclusivity and contractual restrictions on disclosure. Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our drug candidates, manufacturing and process discoveries and other know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. As a normal course of business, we pursue composition-of-matter and method-of-use patents for our product candidates in key therapeutic areas. As of March 1, 2015, we are the owner of record of four issued

or allowed U.S. patents and eight issued or allowed non-U.S. patents, and we are actively pursuing an additional two U.S. patent applications and 18 non-U.S. patent applications. We also rely on trade secrets and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Currently our Hydros platform is covered by three patent families: (1) those relating to modified hyaluronic acid polymer compositions and related methods; (2) those relating to in-situ gel forming compositions; and (3) those relating to stabilized compositions of hyaluronic acid. For the modified hyaluronic acid polymer compositions and related methods patent family which covers the Hydros and Hydros-TA products, we have two issued U.S. patents and four issued non-U.S. patents, all of which will expire in 2030. These patents consist of composition of matter claims, method claims and product-by-process claims. We have issued patents and patent applications that cover Hydros-TA in the United States and 15 countries internationally.

For the patent family relating to in-situ gel forming compositions, we have one granted and one allowed non-U.S. patents and seven pending patent applications in the United States and internationally. Patents in this patent family will expire 2032. For the patent family relating to stabilized compositions of hyaluronic acid, an international patent application and a foreign application have been filed. We have one granted U.S. patent, one allowed U.S. patent application and one pending foreign counterpart in two other different patent families not related to Hydros. These applications cover cross-linking chemistry that is different to that used in the Hydros Platform and are not relevant to the current programs that are in development.

Trade Secrets and Proprietary Information

During the development of the Hydros and Hydros-TA formulations, we have established numerous trade secrets that relate to the raw materials, formulation, manufacturing process and quality control testing of the product. We seek to protect our proprietary information, including our trade secrets and proprietary know-how, by requiring our employees to execute confidentiality and invention assignment agreements upon the commencement of their employment. Consultants and other advisors are required to sign confidentiality and consulting agreements. These agreements generally provide that all confidential information developed or made known during the course of the relationship with us be kept confidential and not be disclosed to third parties except in specific circumstances. In the case of our employees, the agreements also typically provide that all inventions resulting from work performed for us, utilizing our property or relating to our business and conceived or completed during employment shall be our exclusive property to the extent permitted by law. Further, we require confidentiality agreements from entities that receive our confidential data or materials or that generate confidential information and materials for us.

Government Regulation and Product Approval

Government authorities in the United States at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing. Hydros and Hydros-TA and any other drug candidate that we develop must be approved by the FDA before they may be legally marketed in the United States and by the corresponding foreign regulatory agencies before they may be legally marketed in foreign countries.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act and implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state and local

statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable requirements at any time during the product development process, approval process or after approval may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement of profits or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies in compliance with Good Laboratory Practices, or GLP, or other applicable regulations;
- submission to the FDA of an IND application, which must become effective before human clinical trials in the United States may begin;
- approval by an independent institutional review board, or IRB, for each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with laws and FDA regulations pertaining to the conduct of human clinical studies, collectively referred to as Good Clinical Practices, or GCP, to establish the safety and efficacy of the proposed drug for each intended use;
- development of the product under rigorous development and design controls as stipulated by governing regulations such as 21 CFR 210 and 211, known as current Good Manufacturing Practices, or cGMP.
- submission to the FDA of an NDA for a proposed new drug;
- satisfactory completion of a potential FDA inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA's cGMP requirements, to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the NDA;
- satisfactory completion of a potential review by an FDA advisory committee, if applicable; and
- FDA review and approval of the NDA prior to any commercial marketing, sale or shipment of the drug.

The lengthy process of seeking FDA approval and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources and approvals are inherently uncertain. Notwithstanding the expenditure of time and resources approval is never guaranteed and FDA my grant approval for less than the desired indications. Moreover, the time required to obtain approval, if any, may vary substantially based upon the type, complexity and novelty of the product or disease.

Before testing any compounds with potential therapeutic value in humans, a drug candidate typically undergoes nonclinical testing, also referred to as pre-clinical testing. Pre-clinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the characteristics and potential safety and activity of the drug candidate. The conduct of the pre-clinical tests must comply with federal regulations and requirements including GLP.

An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The IND sponsor must submit the results of pre-clinical tests, together with manufacturing information, analytical data, information about product chemistry, any available clinical data or literature and a proposed clinical protocol, among other things, to the FDA as part of the IND. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin.

A separate submission to an existing IND application must also be made for each successive clinical trial conducted during product The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such trial.

Clinical Studies

Clinical trials involve the administration of the drug candidate to healthy subjects or patients with the target disease under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety. Each protocol must be submitted to the FDA under the IND. Clinical trials must be conducted in accordance with the FDA's regulations. Further, each clinical trial must be reviewed and approved by an IRB at or servicing each institution at which the clinical trial will be conducted before the trial commences at that site. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the Informed Consent Form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until it is completed.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The drug is initially introduced into healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. The drug may also be tested for early evidence of effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted only in patients having the specific disease.

- Phase 2. The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for a specific indication and to determine the dosage tolerance, optimal dosage and dosing schedule for patients having the specific disease.
- Phase 3. The drug is administered to an expanded patient population in adequate and well-controlled clinical trials, typically at geographically dispersed clinical trial sites, to generate sufficient data to statistically confirm the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product. Generally, at least two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA, though a single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances (for example, where the study is a large multicenter trial providing highly reliable and statistically persuasive evidence of an important clinical benefit and confirmation of the result in a second trial would be practically or ethically impossible).

Post-approval studies, also referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and may be required by the FDA as part of the approval process.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points, including prior to submission of an IND, at the end of Phase 2 and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice and for the sponsor and FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to study subjects.

Concurrent with clinical trials, companies may complete additional animal studies, develop additional information about the chemistry and physical characteristics of the drug and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

FDA Review and Approval Processes

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the pre-clinical and clinical studies, together with detailed information relating to the product's chemistry, pharmacology, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is subject to a substantial application user fee and the manufacturer and/or sponsor under an approved NDA are also subject to annual product and establishment user fees.

NDAs for most new drug products are based on two Phase 3 clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for modified formulations or new uses of previously FDA-approved products. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted." If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain pre-clinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review.

The FDA may request additional information before accepting an NDA for filing. In this event, the NDA must be resubmitted with the additional information and is subject to payment of additional user fees. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the Prescription Drug User Fee Act, or PDUFA, the FDA has agreed to certain goals for review of NDAs. For an NDA that does not contain a new molecular entity (NME), FDA endeavors to complete its review of a standard NDA and respond to the applicant within 10 months after submission of the NDA, and to complete its review and respond to a priority review NDA within six months after submission of the NDA. For an NDA that contains an NME, the FDA endeavors to complete its review and respond to the applicant within 12 months after submission of a standard NDA and within eight months after submission of a priority review NDA. The FDA does not always meet its PDUFA goal dates for review of standard or priority review NDAs. The review process and the PDUFA goal date may be extended by additional three month review periods whenever the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission at any time during the review cycle.

The FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes independent clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

During the drug approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without a REMS, if required, and the sponsor must agree to the REMS at the time of approval. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate healthcare providers of the drug's risks, limitations on who may prescribe or dispense the drug, or other elements to assure safe use, such as special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. In addition, the REMS must include a timetable to periodically assess the strategy. The requirement for a REMS can materially affect the potential market and profitability of a drug

Before approving an NDA, the FDA may inspect the facilities at which the product is to be manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with FDA regulations regarding conduct of clinical trials. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will inform the applicant of the deficiencies and often will request additional testing or information.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a "complete response" letter, or CRL. The FDA will issue a CRL to indicate that the review cycle for an application is complete and that the application is not ready for approval. A CRL generally describes the specific deficiencies in the NDA identified by the FDA and outlines the additional steps that would need to be undertaken in order for FDA to reconsider the application. These could include additional clinical trials, additional manufacturing or product characterization, or further pre-clinical or pharmacokinetic studies. If a CRL is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. If, or when, the deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. Should the applicant disagree with the decision to issue the CRL, there are dispute resolution processes through which the applicant can appeal the approvability of the NDA

within the FDA. These processes can be lengthy and do not ensure that the NDA will be re-reviewed in its current state or subsequently approved.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require post-approval surveillance to monitor the drug's safety or efficacy or post-approval studies, referred to as Phase 4 studies, which involve clinical trials designed to further assess a product's safety and effectiveness. The FDA has the authority to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Post-Approval Requirements

Any drug products for which we receive FDA approvals will be subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to drug listing and registration, record-keeping, adverse event reporting, reporting updated safety and efficacy information, sampling and distribution and product promotion and advertising. These promotion and advertising requirements include, among other things, standards and regulations regarding direct-to-consumer advertising, prohibitions against promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use") and rules for conducting industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. While physicians may prescribe for off-label uses, manufacturers may only promote their products for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Failure to comply with FDA requirements can have negative consequences, including adverse publicity, enforcement letters from the FDA, mandated corrective advertising or communications with doctors and civil or criminal penalties. In addition, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Manufacturers of our products are required to comply with applicable FDA manufacturing requirements contained in the FDA's cGMP regulations, and quality-control, drug manufacture, packaging and labeling procedures must continue to conform to cGMP regulations after approval. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are also required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced and announced inspections by the FDA and certain state agencies to assess compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Failure to comply with regulatory standards, the emergence of problems following initial marketing, or the discovery of previously unrecognized problems with a product after approval may result in restrictions on a product or the manufacturer or holder of an approved NDA. These restrictions may include suspension of a product until the FDA is assured that quality standards can be met, continuing oversight of manufacturing by the FDA under a consent decree of permanent injunction, which frequently includes the imposition of costs and continuing inspections over a period of many years, as well as possible withdrawal of product approvals or a request for product recalls. The FDA may also impose a REMS requirement on a drug already on the market if the FDA determines, based on new safety information, that a REMS is necessary to ensure that the drug's benefits outweigh its risks. In addition, regulatory authorities may take other enforcement action, including, among other things, warning letters, the seizure of products, refusal to approve pending applications or supplements to approved applications, civil penalties and criminal prosecution.

Changes to the manufacturing process generally require prior FDA approval before being implemented. Other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval. In addition, the distribution of prescription pharmaceuticals is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. A growing majority of states also impose certain drug pedigree requirements on the sale and distribution of prescription drugs.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. Many commercial health plans may also require prior authorization to monitor compliance with patient selection and other coverage criteria.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

In addition to uncertainties surrounding coverage policies, there are periodic changes to reimbursement. Third-party payors regularly update reimbursement amounts and also from time to time revise the methodologies used to determine reimbursement amounts. This includes annual updates to payments to physicians and hospitals where our product candidates will be used. Because injection of the viscosupplement is performed by the physician, usually in the office or outpatient clinic, payors generally reimburse the physician for both the IA injection pursuant to a fee schedule and for the viscosupplement on the basis of the average selling price of each viscosupplement product plus a percentage, the total of which, for Medicare patients, is approximately 106% of the average selling price of each viscosupplement product. As a result, these payment updates could directly impact the demand for our product candidates, if approved. An example of payment updates is the Medicare program's updates to hospital and physician payments, which are done on an annual basis using a prescribed statutory formula. In the past, when the application of the formula resulted in lower payment, Congress has passed interim legislation to prevent the reductions. Most recently, the Protecting Access to Medicare Act of 2014, signed into law in April 2014, provided for a 0.5% update from 2013 payment rates under the Medicare Physician Fee Schedule through 2014 and a 0% update from January 1 until April 1, 2015. If Congress fails to intervene to prevent the negative update factor in future years, the resulting decrease in payment may adversely affect our revenues and results of operations.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the

company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Reform

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reduce healthcare costs.

By way of example, in March 2010, the President signed one of the most significant healthcare reform measures in decades. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively known as the Affordable Care Act, substantially changes the way healthcare will be financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. The comprehensive $940 billion dollar overhaul is expected to extend coverage to approximately 32 million previously uninsured Americans. The Affordable Care Act contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse, which will impact existing government healthcare programs and will result in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program. Additionally, the Affordable Care Act:

- mandates a further shift in the burden of Medicaid payments to the states;
- increases the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%;
- addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- requires collection of rebates for drugs paid by Medicaid managed care organizations;
- requires manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D; and
- imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell “branded prescription drugs” to specified federal government programs.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation’s automatic reduction to several government programs. This includes reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013, and will stay in effect through 2024 unless congressional action is taken. On January 2, 2013, the American Taxpayer

Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates if approved, or additional pricing pressure.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, our activities are potentially subject to regulation under various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

- the federal transparency laws, including the federal Physician Payment Sunshine Act, that requires drug manufacturers to disclose payments and other transfers of value provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

- HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH Act, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities in the future could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the Affordable Care Act broadened the reach of the fraud and abuse laws by, among other things, amending the

intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, exclusion from participation in government healthcare programs, such as Medicare and Medicaid and imprisonment, damages, fines and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We are also subject to the Foreign Corrupt Practices Act, or FCPA, which prohibits improper payments or offers of payments to foreign governments and their officials for the purpose of obtaining or retaining business. Safeguards we implement to discourage improper payments or offers of payments by our employees, consultants and others may be ineffective, and violations of the FCPA and similar laws may result in severe criminal or civil sanctions, or other liabilities or proceedings against us, any of which would likely harm our reputation, business, financial condition and result of operations.

U.S. Marketing Exclusivity

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Act, Congress established abbreviated FDA approval procedures for drugs that are shown to be equivalent to proprietary drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. In support of such applications, a generic manufacturer may rely on the pre-clinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must generally find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug. . . ." In certain situations, an applicant may obtain ANDA approval of a generic product with a strength or dosage form that differs from a referenced innovator drug pursuant to the filing and approval of an ANDA Suitability Petition. The FDA will approve the generic product as suitable for an ANDA application if it finds that the generic product does not raise new questions of safety and effectiveness as compared to the innovator product. A product is not eligible for ANDA approval if the FDA determines that it is not equivalent to the referenced innovator drug, if it is intended for a different use, or if it is not subject to an approved Suitability Petition. However, such a product might be approved under an NDA, with supportive data from clinical trials.

Upon approval of an ANDA, the FDA indicates that the generic product is "therapeutically equivalent" to the RLD and it assigns a therapeutic equivalence rating to the approved generic drug in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists generally consider an "AB" therapeutic equivalence rating to mean that a generic drug is fully

substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, FDA's designation of an "AB" rating often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Non-Patent Exclusivity

The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity, which is a drug that contains an active moiety that has not been approved by the FDA in any other NDA. An "active moiety" is defined as the molecule or ion responsible for the drug substance's physiological or pharmacologic action. In cases where such exclusivity has been granted, an ANDA or 505(b)(2) application referencing that drug may not be filed with the FDA until the expiration of five years after the approval date of the referenced drug, unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the approval date of the referenced drug. The FDCA also provides for a period of three years of exclusivity for a particular condition of approval, or change to a marketed product such as a new formulation for a previously approved product, if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. In cases where such exclusivity is granted, the FDA would be precluded from approving any ANDA or 505(b)(2) application for the protected modification until after that three-year exclusivity period has run. However, unlike NCE exclusivity, the FDA can accept an application and begin the review process during the exclusivity period.

A 505(b)(2) NDA applicant also may be eligible for its own regulatory exclusivity period, such as three-year exclusivity. The first approved 505(b)(2) applicant for a particular condition of approval, or change to a marketed product, such as a new extended release formulation for a previously approved product, may be granted three-year Hatch-Waxman exclusivity if one or more clinical studies, other than bioavailability or bioequivalence studies, was essential to the approval of the application and was conducted/sponsored by the applicant. Should this occur, the FDA would be precluded from making effective any other application for the same condition of use or for a change to the drug product that was granted exclusivity until after that three-year exclusivity period has run. Additional exclusivities may also apply to products approved through the 505(b)(2) pathway.

Hatch-Waxman Patent Certification and the 30-Month Stay

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Upon approval of the NDA, each of the patents listed by the NDA sponsor is published in the Orange Book. When an applicant files an application with the FDA seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the applicant is not seeking approval.

Specifically, the applicant must certify with respect to each patent that:

- no patent information on the drug product that is the subject of the application has been submitted to the FDA;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted.

If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) application will not be approved until all the listed patents claiming the referenced product have expired.

A certification that the listed patent is invalid, unenforceable or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted is known as a Paragraph IV certification. If the ANDA or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or 505(b)(2) application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) application until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, the date of a settlement order or consent decree entered by the court stating that the patent is invalid or not infringed, or a court finding that the patent is invalid or infringed.

Europe/Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a clinical trial application, or CTA, must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, the clinical trial described in that CTA may proceed.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with the ICH GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. In the European Economic Area, or EEA (which is comprised of the 27 Member States of the European Union plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations: the Community MA, which is issued by the European Commission through the Centralized Procedure based on the opinion of the Committee for Medicinal Products for Human Use, a body of the European Medicines Agency, or the EMA, and which is valid throughout the entire territory of the EEA; and the National MA, which is issued by the competent authorities of the Member States of the EEA and only authorized marketing in that Member State's national territory and not the EEA as a whole.

The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. The National MA is for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized

Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member state, or RMS. If the RMS proposes to authorize the product, and the other Member States do not raise objections, the product is granted a national MA in all the Member States where the authorization was sought. Before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Employees

As of March 1, 2015, we had 14 employees. None of our employees is represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Facilities

Our headquarters is currently located in Palo Alto, California, and consists of approximately 16,065 square feet of space, consisting of 10,155 square feet used primarily for our corporate offices and laboratory operations and 5,910 square feet that we sublease. The current term of our lease expires in February 2016. We intend to relocate to a new facility prior to the expiration of our existing lease. We believe that a suitable new facility will be available on commercially reasonable terms.

Legal Proceedings

We are not currently a party to any material legal proceedings.

Management

Executive Officers and Directors

The following table sets forth certain information regarding our executive officers and directors as of March 1, 2015:

Name	Age	Position(s)
Executive Officers and Key Employees		
David M. Renzi	57	President, Chief Executive Officer and Director
T. Michael White	40	Chief Financial Officer and Vice President, Finance
Marcee M. Maroney	45	Vice President, Clinical Affairs
David M. Gravett, Ph.D.	48	Vice President, Research & Development
Hayley Lewis, RAC	39	Vice President, Regulatory Affairs & Quality Assurance
Non-Employee Directors		
Steven L. Basta(1)(3)	49	Director
Albert Cha, M.D., Ph.D.(2)	42	Director
David M. Clapper(3)	63	Director
Keith A. Katkin(2)(3)	43	Director
Guy P. Nohra(2)	54	Director
Edward W. Unkart(1)	65	Director
Reza Zadno, Ph.D.(1)	59	Director

(1) Member of the audit committee.

(2) Member of the compensation committee.

(3) Member of our nominating and corporate governance committee.

Executive Officers

David M. Renzi has served as our president and chief executive officer and as a member of our board of directors since June 2013. From May 2009 to December 2012, Mr. Renzi served as president and chief executive officer of Neomend, a privately-held company that developed and commercialized sprayable surgical sealants and anti-adhesion products, which was acquired by C.R. Bard in December 2012. From January 2005 to December 2008, Mr. Renzi served as the vice president of sales and marketing and the chief commercial officer of SurgRx, a medical device company acquired by the Ethicon Endo-Surgery division of Johnson & Johnson, a medical company, in October 2008. From June 2000 to December 2004, Mr. Renzi served as vice president of sales and marketing and chief marketing officer at Cytyc Surgical Products (formerly Novacept), a medical device company. From 1983 to 1997, Mr. Renzi held various sales and marketing positions at Ethicon Endo-Surgery, a medical company. Mr. Renzi received his B.S. in marketing from Indiana University. We believe Mr. Renzi is qualified to serve on our board of directors because, as our chief executive officer, Mr. Renzi manages and oversees all facets of our operations and also because Mr. Renzi has experience serving as an officer and member of the board of directors of other companies.

T. Michael White has served as our chief financial officer and vice president of finance since July 2014. From February 2014 to June 2014, Mr. White served as an independent consultant. From June 2008 to January 2014, Mr. White served as a vice president and director in the healthcare investment banking group at Barclays, a financial services company, advising clients on a variety of strategic alternatives including equity and debt capital raises and mergers and acquisitions. From August 2002 to June 2008, Mr. White served in a series of positions of increasing responsibility in the healthcare investment banking group at Bear, Stearns & Co. Inc., a financial services company. Mr. White received his B.S. in Finance from the University of Alabama and his M.B.A. from the University of Chicago.

Marcee Maroney has served as our vice president of clinical affairs since June 2008. Ms. Maroney joined us as vice president of marketing in February 2006. From April 2003 to February 2006, Ms. Maroney served as a group manager at Baxter Healthcare, a healthcare company. Ms. Maroney received a B.S. in Physiology and an M.S. in Immunology, both from San Jose State University.

David M. Gravett, Ph.D. has served as our vice president of research and development since October 2007. Dr. Gravett joined us as a senior chemist in March 2007. From 2004 to 2007, Dr. Gravett served as vice president of formulations and polymer chemistry at Angiotech Pharmaceuticals, a medical drug and device company. Dr. Gravett received his BSc and MSc in Chemistry at the University of Natal, South Africa and a Ph.D. in Physical Chemistry from the University of Toronto in Canada.

Hayley Lewis, RAC has served as our vice president of regulatory affairs and quality assurance since May 2014. From May 2003 to May 2014, Ms. Lewis held positions of increasing responsibility at Depomed, a pharmaceutical company, most recently as its senior director of regulatory affairs. Ms. Lewis received a B.S. in Pharmaceutical Sciences from the University of Greenwich in England.

Non-Employee Directors

Steven L. Basta has served as a member of our board of directors since September 2009. Since October 2011 Mr. Basta has served as chief executive officer of AlterG, a privately-held medical device company. From November 2002 to February 2010, Mr. Basta served as chief executive officer of BioForm Medical, a medical aesthetics company, and from February 2010 to September 2011 served as chief executive officer of Merz Aesthetics, the successor to BioForm Medical. Mr. Basta received a B.A. from The Johns Hopkins University and a Master of Management degree from the Kellogg Graduate School of Management at Northwestern University. We believe Mr. Basta is qualified to serve on our board because of his extensive experience in leadership and management roles at various life sciences companies.

Albert Cha, M.D., Ph.D. has served as a member of our board of directors since November 2007. In September 2000, Dr. Cha joined Vivo Capital, a healthcare investment firm, where he has served in various positions, most recently as a managing partner. Dr. Cha currently serves as a member of the boards of directors of several privately-held biotechnology and medical device companies. Dr. Cha received a B.S. and an M.S. from Stanford University and an M.D. and a Ph.D. from the University of California at Los Angeles. We believe Dr. Cha is qualified to serve on our board because of his medical background, venture capital experience and significant experience serving as a director of other life sciences companies.

David M. Clapper has served as a member of our board of directors since December 2014. Since May 2011, Mr. Clapper has served as the chief executive officer of Minerva Surgical, a medical device company. Mr. Clapper previously served as the president and chief executive officer of SurgRx, a privately held medical device manufacturer, from January 2005 to December 2008, when it was sold to Ethicon Endo-Surgery, a Johnson & Johnson Company. From November 1999 to March 2004, Mr. Clapper served as the president and chief executive officer of Novacept, a medical device company that was acquired by Cytyc, a medical device company. Mr. Clapper currently serves as a member of the boards of directors of SVB Financial Group and several privately held medical device and life sciences companies. Mr. Clapper received a B.A. in Marketing from Bowling Green State University. We believe Mr. Clapper is qualified to serve on our board because of his extensive experience serving as a director of other life sciences companies, as well as his extensive experience leading life science companies at a similar stage of development to our own.

Keith A. Katkin has served as a member of our board of directors since December 2014. Mr. Katkin is currently president, chief executive officer and a member of the board of directors of Avanir Pharmaceuticals, a publicly traded pharmaceutical company. Mr. Katkin joined Avanir in July of 2005 as senior vice president of sales and marketing. From 2003 to 2005, Mr. Katkin served as Vice President of Commercial Development for Peninsula Pharmaceuticals, a pharmaceutical company, playing a key role in the 2005 sales of the company to

Johnson & Johnson. Mr. Katkin received a B.S. in Business and Accounting from Indiana University and an M.B.A. in Finance from the Anderson School of management at UCLA. Mr. Katkin became a licensed Certified Public Accountant in 1995. We believe Mr. Katkin is qualified to serve on our board because of his substantial operational leadership experience in the pharmaceutical industry.

Guy P. Nohra has served as a member of our board of directors since December 2005. In March 1996, Mr. Nohra co-founded Alta Partners, a life sciences venture capital firm, and he has since been involved in the funding and development of numerous medical technology and life sciences companies. Mr. Nohra currently serves as a member of the boards of directors of several privately-held life sciences companies. Mr. Nohra received a B.A. in History from Stanford University and an M.B.A. from the University of Chicago. We believe Mr. Nohra is qualified to serve on our board because of his extensive experience in the life sciences industry, his investment and development experience, and his service as a director of other life sciences companies.

Edward W. Unkart has served as a member of our board of directors since December 2014. From August 2006 to August 2009, Mr. Unkart served as a member of the board of directors of XTENT, a publicly traded manufacturer of drug-eluting stent systems. From October 2004 to June 2009, Mr. Unkart served as a member of the board of directors of VNUS Medical Technologies, a publicly traded medical device company, where he was the chair of the company's audit committee and a member of the compensation committee. From January 2005 to December 2008, Mr. Unkart served as vice president of finance and administration and chief financial officer of SurgRx, a manufacturer of medical devices. Mr. Unkart also currently serves on the board of directors of a privately held medical device company. Mr. Unkart is a Certified Public Accountant and holds a B.S. and an M.B.A. from Stanford University. We believe Mr. Unkart is qualified to serve on our board of directors because of his finance and accounting expertise and education and his experience gained through his board and officer positions at other life sciences companies.

Reza Zadno, Ph.D. has served as a member of our board of directors since March 2013. Since January 2015, Dr. Zadno has served as an executive in residence at InterWest Partners, a venture capital firm, where he served as a venture partner from January 2012 to December 2014. From January 2011 to January 2012, Dr. Zadno served as a venture partner at New Leaf Venture Partners, a venture capital firm. From March 2001 to September 2009, Dr. Zadno was founder, president, and chief executive officer of Visiogen, a medical device company, which was acquired by Abbott-Medical Optics, a medical supply company, in 2009, at which time Dr. Zadno served as its general manager until January 2011. Dr. Zadno currently serves as a member of the boards of directors of several privately-held life sciences companies. Dr. Zadno received a Ph.D. (Docteur-Ingenieur) from Ecole des Mines de Paris. We believe Dr. Zadno is qualified to serve on our board because of his medical background, venture capital experience and his leadership and management experience.

Board Composition

Our business and affairs are organized under the direction of our board of directors, which currently consists of eight members. The primary responsibilities of our board of directors are to provide oversight, strategic guidance, counseling and direction to our management. Our board of directors meets on a regular basis and additionally as required.

Our board of directors has determined that all of our directors other than David Renzi are independent directors, as defined by Rule 5605(a)(2) of the Nasdaq Listing Rules.

Effective upon the closing of this offering, we will divide our board of directors into three classes, as follows:

- Class I, which will consist of Albert Cha and Guy Nohra, whose terms will expire at our annual meeting of stockholders to be held in 2016;

- Class II, which will consist of Reza Zadno, Steven Basta and David Clapper whose terms will expire at our annual meeting of stockholders to be held in 2017; and

- Class III, which will consist of David Renzi, Keith Katkin and Ed Unkart, whose terms will expire at our annual meeting of stockholders to be held in 2018.

At each annual meeting of stockholders to be held after the initial classification, the successors to directors whose terms then expire will serve until the third annual meeting following their election and until their successors are duly elected and qualified. The authorized size of our board of directors is eight members. The authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed between the three classes so that, as nearly as possible, each class will consist of one-third of the directors. This classification of the board of directors may have the effect of delaying or preventing changes in our control or management. Our directors may be removed for cause by the affirmative vote of the holders of at least 66 $^{2}/_{3}$% of our voting stock.

Board Leadership Structure

Our bylaws provide our board of directors with flexibility to combine or separate the positions of chairman of the board and chief executive officer in accordance with its determination that utilizing one or the other structure would be in our best interests. At the current time, we do not have a chairman of the board. Our board of directors believes that oversight of our company is the responsibility of our board of directors as a whole, and this responsibility can be properly discharged without a chairman. Our chief executive officer, Mr. Renzi, facilitates communications between members of our board of directors and works with our senior management in the preparation of the agenda for each board meeting. All of our directors are encouraged to make suggestions for board of director's agenda items or pre-meeting materials.

Role of the Board in Risk Oversight

One of the key functions of our board of directors is informed oversight of our risk management process. The board of directors does not have a standing risk management committee, but rather administers this oversight function directly through the board of directors as a whole, as well as through various standing committees of our board of directors that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure and our audit committee has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management is undertaken. The audit committee also monitors compliance with legal and regulatory requirements. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee. Directors serve on these committees until their resignation or until otherwise determined by our board of directors. Copies of our audit committee, compensation committee and nominating and corporate governance committee charters will be available on our website at www.carbylan.com. The reference to our web address does not constitute incorporation by reference of the information contained on or available through our website.

Audit Committee

Our audit committee consists of Steven Basta, Ed Unkart and Reza Zadno. Mr. Unkart serves as the chair of our audit committee. Our board of directors has determined that each of the members of our audit committee

satisfies Nasdaq and SEC independence requirements. The functions of this committee, upon closing of this offering, will include, among other things:

with respect to the auditors,

- exercising sole authority to appoint, compensate, retain, terminate, oversee and evaluate the activities of the auditors;
- having a constructive and positive working relationship with the auditors;
- ensuring that it receives from the auditors a formal written statement delineating all relationships between the auditors and our company, actively engaging in a dialogue with the auditors with respect to any disclosed relationships or services that may impact the objectivity and independence of the auditors, or recommending that our board of directors take appropriate action to oversee the independence of the auditors;
- at least annually, obtaining and reviewing a report by the independent auditors describing: the firm's internal quality-control procedures; any material issues raised by the most recent internal quality-control review or peer review of the firm, or by any inquiry or investigation by governmental or professional authorities, within the preceding five years, respecting one or more independent audits carried out by the firm, and any steps taken to deal with any such issues;
- meeting with the independent auditors prior to the annual audit to discuss planning and staffing of the audit;
- setting clear hiring policies for employees or former employees of the auditors, including but not limited to, those required by all applicable laws and listing rules;
- reviewing and approving the retention of the auditors for the performance of all audit and lawfully permitted non-audit services and the fees and other compensation for such services;
- reviewing with representatives of the auditors: (i) the proposed audit scope, approach and independence, (ii) the auditors' periodic peer review, (iii) the financial statements and audit findings, (iv) any reports prepared by the auditors relating to significant financial reporting issues and judgments, and (v) other applicable matters required to be discussed by generally accepted auditing standards and applicable SEC and listing requirements and rules;
- resolving any disagreements between management and the auditors regarding financial reporting;
- conducting a post-audit review of the financial statements and audit findings, including any significant suggestions for improvements provided to management by the auditors;
- directing the auditors to review before filing with the SEC our interim financial statements included in Quarterly Reports on Form 10-Q, using professional standards and procedures for conducting such reviews; and
- evaluating annually the performance and independence of the auditors;

with respect to our financial reporting process,

- overseeing our accounting and financial reporting processes and the audits of our financial statements;
- discussing with our financial management and auditors the annual audited financial statements and quarterly unaudited financial statements, including the disclosures contained under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations," prior to filing our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, respectively, with the SEC;
- reviewing and discussing with our financial management and auditors our policies and procedures concerning earnings press releases and review the type and presentation of information to be included in earnings press releases (paying particular attention to any use of "pro forma" or "adjusted" non-GAAP information), as well as financial information and earnings guidance provided to analysts and rating agencies;

- providing a report in the proxy statement in accordance with the rules and regulations of the SEC;

with respect to our internal audit process, if applicable,

- overseeing the internal audit process and the activities, organizational structure and qualifications of any internal audit department;
- reviewing, in consultation with management, the auditors and the senior internal auditing executive, and approving the annual internal audit plan;
- reviewing, assessing and approving the charter for any internal audit department;
- reviewing significant reports to management prepared by the internal auditing department and management's responses to such reports;
- discussing with the internal audit department any changes to, and the implementation of, the internal audit plan and any special projects and discuss with the internal audit department the results of the internal audits and any special projects;

with respect to our risks and control environment,

- reviewing on a continuing basis the adequacy of our system of internal controls;
- discussing our major business, operational, and financial risk exposures and the guidelines, policies and practices regarding risk assessment and risk management;
- overseeing the process by which management shall design, implement, amend, maintain, and enforce a comprehensive system of financial controls (including the right internal and external people and resources, policies, processes and enforcement) aimed at ensuring the integrity and compliance of our books and records with generally accepted accounting principles and sound business practices, as well as protecting the value of our assets and safeguarding the credibility of our brand, employees, management team, board of directors, and stockholders;
- overseeing compliance with the requirements of the SEC for disclosure of auditors' services and audit committee members, member qualifications and activities;
- establishing procedures for receiving, retaining and treating complaints we received regarding accounting, internal accounting controls or auditing matters and procedures for the confidential, anonymous submission by employees of concerns regarding questionable accounting or auditing matters;
- investigating, in conjunction with counsel, any legal matter that could have a significant impact on our financial statements or any matter brought to its attention within the scope of its duties;

with respect to other matters:

- reviewing all related party transactions and ensuring they are disclosed as required by applicable law in the financial report that SEC rules require be included in our annual proxy statement;
- reviewing and reassessing the adequacy of the committee charter on an annual basis;
- reviewing reports and any financial information we submitted to the public;
- reporting to our board of directors the matters discussed at each committee meeting;

- performing an evaluation of its performance from time to time to determine whether it is functioning effectively; and

- performing any other activities consistent with the committee charter, the bylaws and governing law as our board of directors and this committee shall deem appropriate.

Our board of directors has determined that Mr. Unkart qualifies as an audit committee financial expert within the meaning of SEC regulations and meets the financial sophistication requirements of the Nasdaq Listing Rules. In making this determination, our board has considered Mr. Unkart's previous and current experience. Both our independent registered public accounting firm and management periodically meet privately with our audit committee.

Compensation Committee

Our compensation committee consists of Albert Cha, Keith Katkin and Guy Nohra. Dr. Cha serves as the chair of our compensation committee. Our board of directors has determined that each of the members of our compensation committee is a non-employee director, as defined in Rule 16b-3 promulgated under the Securities Exchange Act of 1934, as amended, or Exchange Act, is an outside director, as defined pursuant to Section 162(m) of the Internal Revenue Code of 1986, as amended, or the Code, and satisfies Nasdaq and SEC independence requirements. The functions of this committee, upon closing of this offering, will include, among other things:

- assisting our board of directors in developing and evaluating potential candidates for executive positions (including the chief executive officer) and overseeing the development of executive succession plans;

- reviewing and approving corporate goals and objectives relevant to the chief executive officer and other executive officer compensation, evaluating the performance of the chief executive officer and other executive officers in light of those goals and objectives and, either as a committee or together with the other independent directors (as directed by our board of directors), determining and approving, or recommending to our board of directors for approval, the compensation levels for the chief executive officer and other executive officers based on this evaluation with the deliberations and voting on the chief executive officer's compensation to be conducted without the chief executive officer present;

- making recommendations to our board of directors about the compensation of the directors;

- administering our equity-based plans and management incentive compensation plans and making recommendations to our board of directors about amendments to such plans and the adoption of any new employee incentive compensation plans;

- in its sole discretion, appointing, retaining or obtaining the advice of a compensation consultant, legal counsel or other adviser, which includes the sole authority and direct responsibility to approve such compensation consultant's or other adviser's fees and other retention terms, to oversee the work of and to terminate such compensation consultant or other adviser, and the authority and responsibility to pay from our company funds reasonable compensation to such compensation consultant or other adviser retained by this committee, with such funding to be provided by us, as appropriate, as determined by this committee;

- before selecting or obtaining the advice of a compensation consultant, legal counsel or other adviser (other than in-house legal counsel), considering all factors relevant to the independence of such consultant, counsel or adviser from management, including the factors set forth in the Nasdaq listing standards then in effect and any other applicable laws, rules or regulations;

- producing a compensation committee report on executive compensation for inclusion in our annual proxy statement in accordance with the proxy rules;

- reviewing and assessing the adequacy of this charter and submitting any changes to our board of directors for approval on an annual basis;
- reporting its actions and any recommendations to our board of directors on a periodic basis; and
- annually performing, or participating in, an evaluation of the performance of this committee, the results of which shall be presented to our board of directors.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee consists of Steve Basta, David Clapper and Keith Katkin. Mr. Basta serves as the chair of the committee. Our board of directors has determined that the composition and functioning of our nominating and corporate governance committee complies with all applicable requirements of the Sarbanes-Oxley Act of 2002, NASDAQ and SEC rules and regulations. The functions of this committee, upon closing of this offering, will include, among other things:

- providing independent director oversight of director nominations to enhance investor confidence in the selection of well-qualified director nominees;
- assisting the board in identifying prospective director nominees and recommending to the board of directors the director nominees for each annual meeting of stockholders;
- recommending members for each board committee;
- ensuring that the board is properly constituted to meet its fiduciary obligations to our company and the stockholders and that we follow appropriate governance standards;
- developing and recommending governance principles applicable to our company to the board; and
- overseeing the evaluation of the board and management.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has ever been an executive officer or employee of ours. None of our executive officers currently serves, or has served during the last completed fiscal year, on the compensation committee or board of directors of any other entity that has one or more executive officers serving as a member of our board of directors or compensation committee.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics to be effective as of the closing of this offering that applies to all of our officers, including those officers responsible for financial reporting, directors and employees. We will post a copy of our code of business conduct and ethics, and intend to post amendments to this code, or any waivers of its requirements, on our website at www.carbylan.com, as permitted under SEC rules and regulations. The reference to our web address does not constitute incorporation by reference of the information contained on or available through this site.

Director Nominations

Director nominees will be selected by our nominating and corporate governance committee. The board of directors will also consider director candidates recommended for nomination by our stockholders during such times as they are seeking proposed nominees to stand for election at the next annual meeting of stockholders (or, if applicable, a special meeting of stockholders). Our stockholders that wish to nominate a director for election to our board of directors should follow the procedures set forth in Section 1.2 of our bylaws.

We have not formally established any specific, minimum qualifications that must be met or skills that are necessary for directors to possess. In general, in identifying and evaluating nominees for director, our nominating and corporate governance committee considers educational background, diversity of professional experience, knowledge of our business, integrity, professional reputation, independence, wisdom, and the ability to represent the best interests of our stockholders.

Executive and Director Compensation

Executive Compensation

This section describes the material elements of the compensation, with respect to fiscal year 2014, awarded to, earned by, or paid to (i) our president and chief executive officer, David Renzi, and (ii) our two most highly compensated executive officers (other than our chief executive officer), Michael White, our vice president of finance and chief financial officer, who was hired in June 2014, and Hayley Lewis, our vice president of regulatory affairs and quality assurance, who was hired in May 2014. These executives are collectively referred to in this prospectus as our named executive officers.

Each year, the compensation committee of our board of directors and our board of directors review and determine the compensation of our named executive officers.

This discussion contains forward looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. Actual compensation programs that we adopt may differ materially from currently planned programs as summarized in this discussion. As an “emerging growth company” as defined in the JOBS Act, we are not required to include a Compensation Discussion and Analysis section and have elected to comply with the scaled disclosure requirements applicable to emerging growth companies.

Elements of Executive Compensation

As described further below, the compensation of our named executive officers consists of base salary, annual cash bonuses, equity awards and employee benefits that are made available to all salaried employees. Our named executive officers are also entitled to compensation and benefits upon certain terminations of employment and change in control transactions.

Base Salaries. Base salaries of our named executive officers are reviewed and approved annually by our compensation committee, and adjustments to base salaries are based on individual and corporate performance, anonymous private company compensation surveys, the rate of inflation, internal pay equity considerations and the experience of members of our compensation committee. We do not assign a specific weight to any single factor in making decisions regarding base salary adjustments. In determining base salary, our compensation committee uses each named executive officer’s current level of compensation as the starting point.

In February 2014, the compensation committee increased the base salary for Mr. Renzi to $354,375 from his 2013 base salary of $350,000. In connection with the commencement of their employment, Mr. White and Ms. Lewis entered into letter agreements with us providing for an annual base salary of $275,000 and $245,000, respectively.

Annual Cash Bonuses. Our named executive officers are eligible to receive an annual cash bonus upon the achievement of certain performance objectives. As with base salary, the target annual incentive compensation opportunity for Mr. Renzi was initially established through arm’s-length negotiations when he was hired, taking into account Mr. Renzi’s target bonus opportunity at his prior employer, anonymous private company

compensation surveys and internal pay equity considerations, and his qualifications and experience. For 2014, the annual incentive compensation target for Mr. Renzi was 20% of his base salary. Similarly, in connection with their hire, Mr. White and Ms. Lewis entered into letter agreements that provide for an annual incentive compensation target of 25% of base salary, with any annual bonus earned for fiscal 2014 to be pro-rated for their partial year of service.

Notwithstanding the establishment or achievement of annual corporate and departmental goals for our named executive officers' annual bonuses, the compensation committee retains the discretion to alter the amount of any actual award, to account for unforeseen material developments. Bonuses for 2014 are expected to be determined by our compensation committee in February 2015 and paid in April 2015.

Equity Awards. Our named executive officers have been granted stock options under the our Amended and Restated 2004 Stock Option Plan, as amended on December 19, 2012, which we refer to as our "2004 Plan." See "— Equity and Incentive Plans — 2004 Stock Plan" below for additional details about this plan. Awards are generally subject to four year ratable time-based vesting conditions and, in some cases, performance-based vesting conditions. See "— Outstanding Equity Awards at Fiscal Year-End" below for a description of the vesting and other material terms applicable to awards granted to our named executive officers, including those granted in fiscal year 2014.

In October 2014, Mr. White and Ms. Lewis were granted options to purchase 105,506 and 68,579 shares of our common stock, respectively, that vest as to one quarter of the shares on the first anniversary of their respective hire dates, and thereafter in equal monthly installments over the following 36 months, subject to the executive's continued employment. No stock option grants were made to Mr. Renzi in 2014.

Stock option awards serve to align the interests of our named executive officers with our stockholders because no value is created unless the value of our common stock appreciates after grant. Stock option awards also encourage retention through the use of time-based vesting and the achievement of key strategic goals through the use of performance-based vesting. Pursuant to agreements with Mr. Renzi, Mr. White and Ms. Lewis, all or a portion of the executive's stock option awards will vest automatically upon certain terminations of employment following certain change in control transactions. See "— Potential Payments Upon Termination or Change in Control" below for additional details about these agreements.

The 2004 Plan was replaced by our 2014 Stock Option Plan, which we refer to as the "2014 Plan," in April 2014. As described further below, in connection with this offering, we have adopted a public-company plan, referred to as our 2015 Equity Incentive Plan, or the 2015 Equity Plan.

Benefits. We provide benefits to our named executive officers, which we believe to be competitive for our peer group. These benefits include participation in our 401(k) plan and health and welfare benefit coverage. These benefits are available to all of our salaried employees.

Employment and Letter Agreements. We have entered into an employment agreement with Mr. Renzi and letter agreements with Mr. White and Ms. Lewis, each of which includes severance and change-of-control protections.

Summary Compensation Table

The following table sets forth the compensation earned by our named executive officers in fiscal year 2014.

Name and principal position	Year	Salary[1]	Bonus[2]	Option awards[3]	All other compensation	Total
David Renzi,	2014	$ 384,271	—	—	—	$ 384,271
President and Chief Executive Officer	2013	$ 189,583	$30,625	$ 491,803	—	$ 712,011
Michael White,	2014	$ 133,333	—	$ 504,786	—	$ 638,119
Vice President, Finance and Chief Financial Officer[4]						
Hayley Lewis,	2014	$ 163,333	—	$ 328,111	—	$ 491,444
Vice President, Regulatory Affairs and Quality Assurance[5]						

(1) Salaries include amounts contributed by the named executive officer to our 401(k) plan.

(2) Bonuses for 2014 have not been determined as of the date of this prospectus. We expect that our compensation committee will determine 2014 bonuses, if any, for our named executive officers in April 2015. The 2013 amount shown for Mr. Renzi reflects bonus equal to 75% of his incentive compensation target for fiscal year 2013 (with pro-ration based on his June 2013 hire date), which was paid in April 2014. For more information, please see the section above entitled "Elements of Executive Compensation — Annual Cash Bonuses."

(3) Amounts shown reflect the aggregate grant date fair value of stock options awarded in fiscal 2014 and 2013, computed in accordance with FASB ASC Topic 718 and exclude the value of estimated forfeitures. Amounts shown in fiscal 2013 also reflect the incremental fair value of options that were re-priced during fiscal 2013, computed in accordance with FASB ASC Topic 718. Assumptions used in the calculation of these amounts are included in the notes to our financial statements included elsewhere in this prospectus, which are incorporated herein by reference.

(4) Mr. White became our vice president of finance and chief financial officer effective July 7, 2014.

(5) Ms. Lewis became our vice president of regulatory affairs and quality assurance effective May 12, 2014.

Agreements with our Named Executive Officers

Below are descriptions of the material terms of the employment and letter agreements with our named executive officers.

Employment Agreement with Mr. Renzi. We have entered into an executive employment agreement with Mr. Renzi, effective June 3, 2013. Pursuant to this agreement, Mr. Renzi is entitled to an annual base salary of $350,000, and is eligible to receive a target annual cash performance bonus of 20% of base salary, based upon achievement of performance goals determined by the board of directors in consultation with Mr. Renzi. Mr. Renzi also received an option to purchase 525,825 shares of our common stock, the terms of which are described below under the "Outstanding Equity Awards at Fiscal Year-End" table. Mr. Renzi is also entitled to certain severance and change-of-control benefits, the terms of which are described below under "— Potential Payments Upon Termination or Change in Control."

Letter Agreements with Mr. White and Ms. Lewis. We have entered into letter agreements with Mr. White, dated June 26, 2014, and Ms. Lewis, dated April 18, 2014. Pursuant to the letter agreements, Mr. White is entitled to an annual base salary of $275,000 and Ms. Lewis is entitled to an annual base salary of $245,000, and each is eligible to receive a target annual cash performance bonus of 25% of base salary, based upon achievement of performance goals determined by the board of directors, with any annual bonus earned for fiscal 2014 to be pro-rated for their partial year of service. Mr. White and Ms. Lewis also received options to purchase 105,506 and 68,579 shares of our common stock, respectively, in connection with their commencement of employment, the terms of which are described below under the "Outstanding Equity Awards at Fiscal Year-End" table. Mr. White and Ms. Lewis are also entitled to certain severance and change in control benefits, the terms of which are described below under "— Potential Payments Upon Termination or Change in Control."

Outstanding Equity Awards at Fiscal Year-End

The following table sets forth information regarding equity awards held by our named executive officers as of December 31, 2014. Our named executive officers do not hold any equity awards other than stock options.

	OPTION AWARDS					
Name	Vesting commencement date of options	Number of securities underlying unexercised options exercisable	Number of securities underlying unexercised options unexercisable	Equity incentive plan awards: Number of securities underlying unexercised unearned options	Option exercise price	Option expiration date
David Renzi	6/6/2013	197,184(1)	328,641(1)	—	$ 0.56	6/5/2023
Hayley Lewis	5/12/2014	—	68,579(1)	—	$ 7.00	10/31/2024
Michael White	7/7/2014	—	105,506(1)	—	$ 7.00	10/31/2024

(1) Reflects time-based options to purchase shares of our common stock that vest as to 1/4 of the shares on the one-year anniversary of the vesting commencement date, and thereafter in equal monthly installments over the following 36 months, generally subject to the executive's continued employment.

Retirement Benefits

We do not maintain any qualified or non-qualified defined benefit plans or supplemental executive retirement plans that cover our named executive officers. Our 401(k) plan permits eligible employees to defer their annual eligible compensation subject to certain limitations imposed by the Internal Revenue Service. Our 401(k) plan does not provide for employer contributions.

Potential Payments Upon Termination or Change in Control

Mr. Renzi, Mr. White and Ms. Lewis — Termination of Employment without Cause or for Good Reason. Pursuant to Mr. Renzi's, Mr. White's and Ms. Lewis's employment or letter agreements, as applicable, if the executive's employment is terminated by us without cause or by the executive for good reason (as such terms are defined in the executive's employment agreement or letter agreement, as applicable), the executive will be entitled to (1) continued payment of the executive's base salary for a period of 12 months (for Mr. Renzi) or 6 months (for Mr. White and Ms. Lewis) following such termination of employment, (2) payment of the executive's COBRA premiums until the earliest of 12 months (for Mr. Renzi) or 6 months (for Mr. White and Ms. Lewis) following such termination of employment, the date on which he or she becomes eligible for group health insurance coverage through a new employer, or the date he or she ceases to be eligible for COBRA continuation coverage for any reason, and (3) accelerated vesting as to the portion of his or her stock options that would have vested in the 12-months (for Mr. Renzi) or 6-months (for Mr. White and Ms. Lewis) following such termination of employment had the executive remained employed with the Company. In the event of Mr. White's or Ms. Lewis's death during the 6-month severance period, the remainder of the severance benefits set forth above will be paid to his or her estate.

Notwithstanding the foregoing, the severance benefits for Mr. White and Ms. Lewis will immediately cease in the event that the executive obtains new full-time employment (or a full-time consulting or similar arrangement) within 6 months after the termination date, provided, however, that the Company will thereafter continue to pay the executive, through the 6-month severance payment period, the excess, if any, of the Company base salary on the date of termination over the base salary for the new employment relationship.

Mr. Renzi — Termination of Employment in Connection with a Change in Control. If Mr. Renzi's employment is terminated by us without cause or by him for good reason (as such terms are defined in Mr. Renzi's employment agreement) either three months prior to or within one year following the effective date of a change in control (as such term is defined in Mr. Renzi's employment agreement), in addition to the benefits described above under "*— Mr. Renzi, Mr. White and Ms. Lewis — Termination of Employment without Cause or for Good Reason*," all stock options held by such him will vest in full.

Mr. White and Ms. Lewis — Termination of Employment in Connection with a Change in Control. If Mr. White's or Ms. Lewis's employment is terminated by us without cause or by the executive for good reason (as such terms are defined in the executive's letter agreement) within one year following the effective date of a change in control (as such term is defined in the executive's letter agreement), in addition to the benefits described above under "*— Mr. Renzi, Mr. White and Ms. Lewis — Termination of Employment without Cause or for Good Reason*," (1) all stock options held by such executive will vest in full, and (2) the executive will be eligible to receive a pro-rated bonus payment for the year in which his or her employment terminates, with such bonus amount to be based upon the achievement of the bonus objectives prior to such termination or resignation of employment. The executive will also be entitled to receive the full 6 months' base salary continuation, regardless of whether he or she obtains new full-time employment (or a full-time consulting or similar arrangement).

Mr. Renzi, Mr. White and Ms. Lewis — Severance Subject to Release of Claims and Restrictive Covenants. Our obligation to provide our named executive officers with any severance payments or other benefits under his or her employment agreement or letter agreement, as applicable, is conditioned on the executive signing and not revoking a separation agreement and effective release of claims in our favor. Mr. Renzi is also subject to a 12-month post-termination non-solicitation of employees, independent contractor and consultants.

Director Compensation Policy

Our board of directors has adopted an independent director compensation policy, effective in connection with this offering, which is designed to enable us to attract and retain, on a long-term basis, highly qualified independent directors.

Following this offering, we will pay our independent directors, as well as future independent directors, each a qualifying director, an annual retainer of $35,000. In addition, each qualifying director who serves as the chairperson of our audit committee, compensation committee or nominating and corporate governance committee will receive, for his or her service in such capacity, an additional annual retainer of $15,000, $10,000 or $7,500, respectively, and each other qualifying director who is a member of the audit committee, compensation committee or nominating and corporate governance committee will receive an annual retainer of $7,500, $5,000 or $3,750, respectively. We reimburse each non-employee member of our board of directors for reasonable out-of-pocket expenses incurred in connection with attending our board and committee meetings.

In the past, we have granted independent directors options to purchase our common stock pursuant to the terms of our 2004 Plan and 2014 Plan. Effective upon the closing of this offering, any future director will automatically receive an initial award of an option to purchase 13,750 shares of our common stock under our 2015 Equity Plan. In addition, beginning in 2016, directors who have served for at least the preceding six months will receive an annual grant of an option to purchase 6,250 shares on the day of and immediately following each annual meeting of our stockholders. Each initial option grant will vest in equal monthly installments over the first three years following the date of grant, subject to the director remaining in service on the applicable vesting date. Each annual option grant will be fully vested on the date of grant. Options granted will have an exercise price equal to the fair market value on the date of grant and will have a 10-year term. For a more detailed description of these plans, see "Executive Compensation—Equity and Incentive Plans."

The following table sets forth information concerning the compensation earned by our directors during fiscal year 2014.

DIRECTOR COMPENSATION

Name	Fees earned or paid in cash[1]	Option awards[2]	Total
Steve L. Basta	—	$ 39,494	$ 39,494
David Clapper	—	$ 170,862	$ 170,862
Keith Katkin	—	$ 170,862	$ 170,862
Samuel Lynch[3]	$ 12,500	—	$ 12,500
Edward Unkart	—	$ 170,862	$ 170,862

(1) Other than Mr. Lynch, none of our directors received fees earned or paid in cash for their services in 2014.

(2) Amount shown for each director represents the aggregate grant date fair value of an option to purchase 6,250 shares of our common stock granted to Mr. Basta and 27,039 shares of our common stock granted to each of Messrs. Clapper, Katkin and Unkart in fiscal 2014, at an exercise price of $8.20 per share. These amounts were computed in accordance with FASB ASC Topic 718 and exclude the value of estimated forfeitures. Assumptions used in the calculation of these amounts are included in the notes to our financial statements included elsewhere in this prospectus. As of the end of fiscal year 2014, Mr. Basta held options for 42,090 shares of common stock, Messrs. Clapper, Katkin and Unkart each held options for 27,039 shares of common stock, and Mr. Lynch held options for 51,841 shares of common stock.

(3) Mr. Lynch resigned from our board of directors in April 2014.

In December 2014, Mr. Basta received an option to purchase 6,250 shares of our common stock and each of Messrs. Clapper, Katkin and Unkart received an option to purchase 27,039 shares of our common stock, which vest in equal monthly installments over 36 months on each successive one-month anniversary of the December 2014 vesting commencement date, subject to the director's continued service through each such vesting date. The directors' stock option awards will become fully vested on a change in control of the Company.

Equity and Incentive Plans

2015 Equity Incentive Plan

In January 2015, our board adopted the 2015 Equity Plan and following this offering, all equity-based awards will be granted under the 2015 Equity Plan. As of the date of this prospectus, no awards have been made under the 2015 Equity Plan. The following summary describes the material terms of the 2015 Equity Plan. This summary is not a complete description of all provisions of the 2015 Equity Plan and is qualified in its entirety by reference to the 2015 Equity Plan, which is filed as an exhibit to the registration statement of which this prospectus is a part.

Purpose. The purpose of the 2015 Equity Plan is to advance our interests by providing for the grant to participants of equity incentive awards.

Plan administration. The 2015 Equity Plan will be administered by the compensation committee of our board of directors, or the Administrator. The Administrator will have the authority to, among other things, interpret the 2015 Equity Plan, determine eligibility for, grant and determine the terms of awards under the 2015 Equity Plan, and to do all things necessary to carry out the purposes of the 2015 Equity Plan. The Administrator's determinations under the 2015 Equity Plan will be conclusive and binding.

Authorized shares. Subject to adjustment, the maximum number of shares of our common stock that may be delivered in satisfaction of awards under the 2015 Equity Plan, including shares issuable, but not yet issued, under outstanding awards granted under the 2014 Plan, as well as shares available for future awards, will be 1,524,857 shares. The number of shares available for issuance under our 2015 Equity Plan will be increased on the first day of each fiscal year beginning in 2016, by an amount equal to the least of (1) 1,200,000 shares of stock, (2) four percent (4%) of the outstanding shares of stock on the last day of the immediately preceding

calendar year, and (3) such number of shares of stock, if any, determined by our board of directors to the extent the board takes action with respect to the foregoing (if the board does not take such action, the number of shares of stock shall be increased by the lesser of (1) and (2)).

Shares of common stock to be issued under the 2015 Equity Plan may be authorized but unissued shares of common stock or previously-issued shares. Any shares of common stock underlying awards that are forfeited, surrendered, expire or become unexercisable without having been exercised in full, or that are repurchased or otherwise reacquired by us, will again be available for issuance under the 2015 Equity Plan. In addition, all awards granted under the 2014 Plan and the 2004 Plan, both of which are described below, that are repurchased, forfeited, expired or are cancelled will become available for grant under our 2015 Equity Plan. Any shares of common stock underlying awards that are withheld to cover the exercise price or any applicable tax withholding will not again become available for issuance under the 2015 Equity Plan.

Individual limits. The maximum number of shares for which stock options may be granted and the maximum number of shares of stock subject to stock appreciation rights to any person in any calendar year will each be 1,000,000 shares. The maximum number of shares subject to other awards granted to any person in any calendar year will also be 1,000,000 shares. The maximum value of any cash award granted to any person in any calendar year will be $1,000,000.

Eligibility. The Administrator will select participants from among our key associates, directors, consultants and advisors and its affiliates who are in a position to make a significant contribution to our success. Eligibility for stock options intended to be incentive stock options (ISOs) is limited to our employees or certain affiliates.

Types of awards. The 2015 Equity Plan provides for grants of stock options, stock appreciation rights, restricted and unrestricted stock and stock units, performance awards and other awards convertible into or otherwise based on shares of our stock and cash awards. Dividend equivalents may also be provided in connection with an award under the 2015 Equity Plan.

- *Stock options and stock appreciation rights:* The exercise price of an option, and the base price against which a stock appreciation right is to be measured, are not permitted to be less than the fair market value (or, in the case of an ISO granted to a ten-percent stockholder, 110% of the fair market value) of a share of common stock on the date of grant. The Administrator will determine the time or times at which stock options or stock appreciation rights become exercisable and the terms on which such awards remain exercisable.

- *Restricted and unrestricted stock:* A restricted stock award is an award of common stock subject to forfeiture restrictions, while an unrestricted stock award is not subject to restrictions under the 2015 Equity Plan.

- *Stock units:* A stock unit award is denominated in shares of common stock and entitles the participant to receive stock or cash measured by the value of the shares in the future. The delivery of stock or cash under a stock unit may be subject to the satisfaction of performance conditions or other vesting conditions.

- *Performance awards:* A performance award is an award the vesting, settlement or exercisability of which is subject to specified performance criteria. Performance awards may be stock-based or cash-based.

Vesting. The Administrator will have the authority to determine the vesting schedule applicable to each award, and to accelerate the vesting or exercisability of any award.

Termination of employment. The Administrator will determine the effect of termination of employment or service on an award. Unless otherwise provided by the Administrator or in an award agreement, upon a termination

of employment all unvested options and other awards requiring exercise will terminate, all other unvested awards will be forfeited and vested options will terminate if not exercised within post-termination exercise windows set forth in the 2015 Equity Plan.

Performance criteria. The 2015 Equity Plan will provide that grants of performance awards will be made based upon, and subject to achieving, "performance objectives" over a performance period, which may be one or more periods as established by the Administrator. Performance objectives with respect to those awards that are intended to qualify as "performance-based compensation" for purposes of Section 162(m) are limited to an objectively determinable measure or objectively determinable measures of performance relating to any or any combination of the following (measured either absolutely or by reference to an index or indices and determined either on a consolidated basis or, as the context permits, on a divisional, subsidiary, line of business, project or geographical basis or in combinations thereof): sales; revenues; assets; expenses and cost-reduction goals; budget management; earnings before or after deduction for all or any portion of interest, taxes, depreciation, or amortization, whether or not on a continuing operations or an aggregate or per share basis; return on equity, investment, capital or assets; capital expenditures; one or more operating ratios; borrowing levels, leverage ratios or credit rating; debt reduction; market share; capital expenditures; cash flow; stock price; stockholder return; implementation or completion of projects or processes (including, without limitation, clinical trial initiation, clinical trial enrollment, clinical trial results, new and supplemental indications for existing products, regulatory filing submissions, regulatory filing acceptances, regulatory or advisory committee interactions, regulatory approvals and product supply); user or partner satisfaction; workforce diversity; employee retention; initiation of phases of clinical trials and/or studies by specific dates; patient enrollment rates; submission to, or approval by, a regulatory body (including, but not limited to the U.S. Food and Drug Administration) of an applicable filing or a product candidate; regulatory milestones; progress of internal research or clinical programs; progress of partnered programs; timely completion of clinical trials; submission of INDs and NDAs and other regulatory achievements; research progress, including the development of programs; strategic partnerships or transactions (including in-licensing and out-licensing of intellectual property); sales of particular products or services; customer acquisition or retention; acquisitions and divestitures (in whole or in part); joint ventures and strategic alliances; spin-offs, split-ups and the like; reorganizations; or recapitalizations, restructurings, financings (issuance of debt or equity) or refinancings.

To the extent consistent with the requirements for satisfying the performance-based compensation exception under Section 162(m), the Administrator may provide in the case of any award intended to qualify for such exception that one or more of the performance objectives applicable to an award will be adjusted in an objectively determinable manner to reflect events (for example, but without limitation, acquisitions or dispositions) occurring during the performance period of such award that affect the applicable performance objectives.

Transferability. Awards under the 2015 Equity Plan may not be transferred except by will or by the laws of descent and distribution, unless (for awards other than ISOs) otherwise provided by the Administrator.

Corporate transactions. In the event of a consolidation, merger or similar transaction, a sale or transfer of all or substantially all of our assets or a dissolution or liquidation, the Administrator may, among other things, provide for continuation or assumption of outstanding awards, for new grants in substitution of outstanding awards, for the accelerated vesting or delivery of shares under awards, or for a cash-out of outstanding awards, in each case on such terms and with such restrictions as it deems appropriate. Except as the Administrator may otherwise determine, awards not assumed will terminate upon the closing of such corporate transaction.

Adjustment. In the event of certain corporate transactions (including a stock dividend, stock split or combination of shares, recapitalization or other change in our capital structure, the Administrator will make appropriate adjustments to the maximum number of shares that may be delivered under and the individual limits included in the 2015 Equity Plan, and will also make appropriate adjustments to the number and kind of shares of stock or securities subject to awards, the exercise prices of such awards or any other terms of awards affected by

such change. The Administrator will also make the types of adjustments described above to take into account distributions and other events other than those listed above if it determines that such adjustments are appropriate to avoid distortion and preserve the value of awards.

Amendment and termination. The Administrator will be able to amend the 2015 Equity Plan or outstanding awards, or terminate the 2015 Equity Plan as to future grants of awards, except that the Administrator will not be able alter the terms of an award if it would affect materially and adversely a participant's rights under the award without the participant's consent (unless expressly provided in the 2015 Equity Plan or reserved by the Administrator). Stockholder approval will be required for any amendment to the extent such approval is required by law, including the Code or applicable stock exchange requirements.

Annual Incentive Plan

In January 2015, our board of directors adopted an annual incentive plan, or the Annual Plan. Starting with our 2015 fiscal year, annual award opportunities for certain key employees, including our named executive officers, will be granted under the Annual Plan. The following summary describes what we anticipate to be the material terms of the Annual Plan. This summary is not a complete description of all provisions of the Annual Plan. You are encouraged to read the full text of the Annual Plan, which has been filed as an exhibit to the registration statement of which this prospectus forms a part.

The Annual Plan will be administered by the compensation committee of our board of directors. Executive officers and other key employees of us and our affiliates will be selected from time to time by the compensation committee to participate in the Annual Plan. Award opportunities under the Annual Plan will be granted by the compensation committee prior to, or within a specified period of time following the beginning of, the fiscal year or other performance period selected by the compensation committee. The compensation committee will establish the performance criteria applicable to the award, the amount or amounts payable if the performance criteria are achieved, and such other terms as the compensation committee deems appropriate. Awards granted under the Annual Plan will be exempt from the compensation limitations set forth in Section 162(m) until the earliest of (i) a material modification of the Annual Plan, (ii) our fourth annual stockholders meeting after the completion of this offering, (iii) the expiration of the Annual Plan or (iv) the payment of all of the compensation allocated under the Annual Plan.

Awards under the Annual Plan will be made based on, and subject to achieving, performance criteria established by the compensation committee. Performance criteria for awards intended to qualify as performance-based compensation for purposes of Section 162(m) are limited to the objectively determinable measures of performance relating to any or any combination of the performance criteria set forth above under "— 2015 Equity Incentive Plan." To the extent consistent with the requirements of Section 162(m), the compensation committee may establish, in the case of any award intended to qualify as exempt performance-based compensation under Section 162(m), that one or more of the performance criteria applicable to such award be adjusted in an objectively determinable manner to reflect events occurring during the performance period of such award that affect the applicable performance criteria.

A participant will be entitled to payment under an award only if all conditions to payment have been satisfied under the award. Following the close of the performance period, the compensation committee will determine (and, to the extent required by Section 162(m), certify) whether and to what extent the applicable performance criteria have been satisfied. The compensation committee will then determine the actual payment, if any, under each award. The maximum payment to any participant under the Annual Plan for any fiscal year will in no event exceed $10,000,000. The compensation committee may amend or terminate the Annual Plan at any time, provided that any amendment will be approved by our stockholders if required by Section 162(m).

2014 Stock Option Plan

On April 8, 2014, our board adopted the 2014 Plan. This summary is not a complete description of all provisions of the 2014 Plan and is qualified in its entirety by reference to the 2014 Plan, which is filed as an exhibit to the registration statement of which this prospectus is a part.

Purpose. The purpose of the 2014 Plan is to advance our company's interests by providing for the grant to participants of equity-based awards.

Plan administration. The 2014 Plan is administered by the board of directors or a committee appointed by the board (the "Administrator"). The Administrator has the authority to, among other things, interpret the 2014 Plan, determine eligibility for, grant and determine the terms of awards under the 2014 Plan, and to do all things necessary to carry out the purposes of the 2014 Plan. The Administrator's determinations under the 2014 Plan are conclusive and binding.

Authorized shares. Subject to adjustment, the number of shares of our common stock that may be delivered in satisfaction of awards under the 2014 Plan is 250,000 shares. In addition, shares that remain available for issuance under the 2004 Plan following its expiration, as well as shares that become available for grant under the 2004 Plan following its expiration as a result of the forfeiture of awards granted under such plan, are available for issuance under the 2014 Plan.

Shares of common stock to be issued under the 2014 Plan may be authorized but unissued shares of common stock or previously-issued shares. Any shares of common stock underlying awards that are forfeited, surrendered, expire or become unexercisable without having been exercised in full, or that are repurchased or otherwise reacquired by us, will again be available for issuance under the 2014 Plan. Any shares of common stock underlying awards that are withheld to cover the exercise price or any applicable tax withholding will not again become available for issuance under the 2014 Plan.

Eligibility. The Administrator may select participants from among our key employees, directors, and consultants and its affiliates who are in a position to make a significant contribution to our success. Eligibility for stock options intended to be incentive stock options (ISOs) is limited our employees and certain affiliates.

Types of awards; vesting. The 2014 Plan provides for grants of stock options, certain of which may be exercised prior to vesting at the election of the participant in exchange for an award of restricted stock.

- *Stock options:* The exercise price of an option, and the base price against which a stock appreciation right is to be measured, may not be less than the fair market value (or, in the case of an ISO granted to a ten percent stockholder, 110% of the fair market value) of a share of common stock on the date of grant. The Administrator determines the time or times at which stock options become exercisable and the terms on which such awards remain exercisable. Unless otherwise provided for in an award agreement, all stock options, whether vested or not, expire on the tenth anniversary of their date of grant unless earlier terminated.

- *Restricted stock:* A restricted stock award is an award of common stock subject to forfeiture restrictions.

Termination of employment or service. The Administrator will determine the effect of termination of employment or service on an award. Unless otherwise provided by the Administrator or in an award agreement, upon a termination of employment or service all unvested options will terminate, and vested options will remain outstanding and exercisable for three months, or one year in the case of death or disability, or, in each case, until the applicable expiration date, if earlier. If a participant's employment or service relationship is terminated for cause, as determined by the Administrator, all options held by such participant (whether or not vested) will immediately terminate on the date of such termination. With respect to restricted stock, if a participant's employment or service relationship is terminated for any reason, including death or disability, we will have the right for 90 days to repurchase from the participant the restricted stock at the lesser of the price paid by the participant for such restricted stock or the fair market value of such shares on the repurchase date; if we do not exercise this repurchase right, the repurchase right will terminate.

Transferability. Awards under the 2014 Plan may not be transferred except by will or by the laws of descent and distribution, unless otherwise provided by the Administrator.

Corporate transactions. In the event of a merger, consolidation or similar transaction, or a sale or transfer of all or substantially all of our assets, each outstanding award will be assumed or substituted by the successor entity or parent or subsidiary thereof (collectively, the "successor entity"); provided that if the successor entity refuses such assumption or substitution, each outstanding award will become fully vested in lieu of such assumption or substitution, and each stock option will be exercisable for a period of time determined by the Administrator. In the event of our dissolution or liquidation, each outstanding option will terminate immediately prior to the closing of such transaction.

Adjustment. In the event of certain corporate transactions (including a stock dividend or other distribution, recapitalization, stock split, reverse stock split, reorganization, merger, consolidation, split-up, spin-off, combination, repurchase, or exchange of shares or other securities or other change in the corporate structure affecting the shares), the Administrator may make appropriate adjustments to the number of shares that may be delivered under the 2014 Plan, and will also make appropriate adjustments to the number and kind of shares of stock or securities subject to awards, the exercise prices of such awards.

Amendment and termination. The board may amend the 2014 Plan or outstanding awards, or terminate the 2014 Plan as to future grants of awards. Except as otherwise provided for in the 2014 Plan, the terms of an award cannot be altered if it would affect materially and adversely a participant's rights under the award without the participant's consent (unless expressly reserved by the Administrator at the time of grant). The board will obtain stockholder approval for any amendment to the extent such approval is required by law, including the Code or applicable stock exchange requirements.

2004 Stock Option Plan

Prior to adoption of the 2014 Plan, we granted all equity awards under the 2004 Plan. The 2004 Plan was replaced by the 2014 Plan in April 2014, and no awards have been granted under the 2004 Plan since that time. The terms and conditions of the 2004 Plan are substantially similar to the 2014 Plan, except that, in addition to the types of awards subject to the 2014 Plan, the 2004 Plan provides for the grant of stock purchase rights. As of the date of this prospectus, there are options outstanding to acquire 945,633 shares under the 2004 Plan, and there are no outstanding stock purchase rights.

Limitation of Liability and Indemnification

Our amended and restated certificate of incorporation, which will become effective upon the closing of this offering, limits the liability of directors to the fullest extent permitted by Delaware law as it presently exists or may be amended from time to time. Our directors will not be personally liable for monetary damages for breach of their fiduciary duties as directors, except liability for any of the following acts:

- any breach of their duty of loyalty to the corporation or its stockholders;
- acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not apply to liabilities arising under federal securities laws and do not affect the availability of equitable remedies such as injunctive relief or rescission.

Our amended and restated bylaws, which will become effective upon the closing of this offering, provide that we will indemnify our directors, officers, employees and other agents to the fullest extent permitted by Delaware law or other applicable law. Our amended and restated bylaws also permit us to secure insurance on

behalf of any officer, director, employee or other agent for us, or anybody serving at our request as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise for any liability asserted against such person and incurred by such person in any such capacity, or arising out of such person's status as such, regardless of whether we have the power to indemnify such person against such liability under the provisions of Delaware law. We have obtained an insurance policy that insures our directors and officers against certain liabilities, including liabilities arising under applicable securities laws.

We have entered into separate indemnification agreements with our directors and executive officers, in addition to the indemnification provided for in our amended and restated bylaws. These agreements, among other things, provide that we will indemnify our directors and executive officers for certain expenses, including attorneys' fees, judgments, penalties, fines and settlement amounts incurred by a director or executive officer in any action or proceeding arising out of their services as one of our directors or executive officers, or any of our subsidiaries or any other company or enterprise to which the person provides services at our request. The indemnification agreements also set forth certain procedures that will apply in the event of a claim for indemnification thereunder. At present, there is no pending litigation or proceeding involving any of our directors or executive officers as to which indemnification is required or permitted, and we are not aware of any threatened litigation or proceeding that may result in a claim for indemnification.

Certain Relationships and Related Party Transactions

The following includes a summary of transactions since January 1, 2011 to which we have been a party, in which the amount involved in the transaction exceeded $120,000, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our capital stock or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described under "Executive and Director Compensation."

September 2014 and February 2015 Convertible Note Financing

On September 29, 2014 and February 2015 we entered into convertible note purchase agreement with, and issued convertible promissory notes in an aggregate principal amount of $5.0 million and $4.0 million, respectively, to, several of our affiliates in the amounts set forth below. Immediately prior to the completion of this offering, the convertible promissory notes will automatically convert into a number of shares of our common stock equal to the quotient obtained by dividing the entire principal amount and accrued interest on the convertible promissory notes by 80% of the initial public offering price per share of our common stock.

Investor	September 2014 Note Principal Amount	February 2015 Note Principal Amount
ACP IV, L.P.(1)	$ 1,655,654	$ 1,324,523
InterWest Partners IX, L.P.(2)	1,819,568	1,455,654
Entities affiliated with Vivo Ventures(3)	1,524,778	1,219,823
Total	**$ 5,000,000**	**$ 4,000,000**

(1) Guy P. Nohra, a member of our board of directors, is associated with ACP IV, L.P.

(2) Reza Zadno, Ph.D., a member of our board of directors, is associated with InterWest Partners IX, L.P.

(3) Albert Cha, M.D., Ph.D., a member of our board of directors, is associated with the entities affiliated with Vivo Ventures.

Preferred Stock Financings

December 2012, February 2013 and June 2013 Series B Preferred Stock Financing

The table below sets forth the number of shares of Series B convertible preferred stock sold to our directors, executive officers or owners of more than 5% of a class of our capital stock, or an affiliate or immediate family member thereof:

Investor	Aggregate Series B Shares Sold in December 2012-June 2013 Closings	Aggregate Purchase Price
ACP IV, L.P.(1)	831,531	$ 4,000,000
InterWest Partners IX, L.P.(2)	831,531	$ 4,000,000
Entities affiliated with Vivo Ventures(3)	831,530	$ 4,000,000

(1) Guy P. Nohra, a member of our board of directors, is associated with ACP IV, L.P.

(2) Reza Zadno, Ph.D., a member of our board of directors, is associated with InterWest Partners IX, L.P.

(3) Albert Cha, M.D., Ph.D., a member of our board of directors, is associated with the entities affiliated with Vivo Ventures.

Series B preferred adjustment. In connection with the 2012 and 2013 Series B financing, in December 2012, we approved the adjustment of the Series B preferred stock liquidation preference from $5.52 per share to $4.8104 per share. In order to preserve the aggregate liquidation preference of the holders of pre-2012 issued Series B preferred stock, we issued 534,467 shares of Series B preferred stock to such holders for no payment.

ACP IV, L.P., InterWest Partners IX, L.P., and entities affiliated with Vivo Ventures received 147,781 shares, 168,892 shares and 213,787 shares, respectively, as a result of this adjustment. See Note 7 to our financial statements appearing elsewhere in this prospectus for further details on the issuance of additional Series B convertible preferred stock.

Participation in this Offering

Certain of our existing institutional investors, including investors affiliated with certain of our directors, have agreed to purchase an aggregate of 2,700,000 shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering. See the footnotes to the beneficial ownership table in “Principal Stockholders” for more details.

Registration Rights

We have entered into an amended and restated registration rights agreement with purchasers of our preferred stock and warrants to purchase preferred stock that provides for certain rights relating to the registration of their shares of common stock issuable upon conversion of their preferred stock and warrants to purchase preferred stock, as applicable. These rights will continue following this offering and will terminate no later than seven years following the closing of this offering, or for any particular holder with registration rights, at such time following this offering when all securities held by that stockholder subject to registration rights may be sold pursuant to Rule 144 under the Securities Act. All holders of our preferred stock and warrants to purchase preferred stock, as applicable, are parties to this agreement. See “Description of Capital Stock — Registration Rights” for additional information.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. These agreements require us to indemnify these individuals and, in certain cases, affiliates of such individuals, to the fullest extent permissible under Delaware law against liabilities that may arise by reason of their service to us or at our direction, and to advance expenses incurred as a result of any proceeding against them as to which they could be indemnified.

Policies and Procedures for Transactions with Related Persons

We have adopted a related person transaction approval policy that will govern the review of related person transactions following the closing of this offering. Pursuant to this policy, if we want to enter into a transaction with a related person or an affiliate of a related person, our chief financial officer will review the proposed transaction to determine, based on applicable Nasdaq and SEC rules, if such transaction qualifies as a related person transaction. If the chief financial officer determines that the proposed transaction is a related person transaction, then the proposed transaction shall be submitted to the audit committee for pre-approval at the next regular or special audit committee meeting; if the chief financial officer, in consultation with the chief executive officer, determines that it is not practicable to wait until the next meeting of the audit committee, then the chief financial officer may submit the proposed transaction to the chairperson of the audit committee. In the event that our chief executive officer or chief financial officer becomes aware of a related person transaction that has not been previously approved or previously ratified under our related person transaction approval policy, the transaction, if ongoing, will be promptly submitted to the audit committee or the chairperson of the audit committee for consideration. If the transaction is already completed, the audit committee or the chairperson of the audit committee shall evaluate the transaction to determine if rescission of the transaction and/or any disciplinary action is appropriate.

Principal Stockholders

The following table sets forth certain information regarding the beneficial ownership of our common stock as of March 1, 2015 with respect to:

- each person known by us to beneficially own 5% or more of the outstanding shares of our common stock;
- each member of our board of directors and each named executive officer; and
- the members of our board of directors and our current executive officers as a group.

Unless otherwise noted below, the address of each beneficial owner listed in the table below is c/o Carbylan Therapeutics, Inc., 3181 Porter Drive, Palo Alto, CA 94304.

We have determined beneficial ownership in accordance with the rules of the SEC. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons and entities named in the table below have sole voting and investment power with respect to all shares of common stock that he or she beneficially owns, subject to applicable community property laws.

Certain of our existing institutional investors, including investors affiliated with certain of our directors, have agreed to purchase an aggregate of 2,700,000 shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering. The figures in the table below reflect the purchase of the shares in this offering by these investors in the amounts they have agreed to purchase.

Each stockholder's percentage ownership before the offering is based on 8,976,987 shares of our common stock outstanding as of March 1, 2015, assuming (1) the automatic conversion of all outstanding shares of our preferred stock into 8,268,531 shares of common stock, and (2) excluding the exercise of any outstanding warrants. Each stockholder's percentage ownership after the offering is based on 24,264,107 shares of our common stock to be outstanding after this offering, assuming (1) the automatic conversion of all outstanding shares of our preferred stock into 8,268,531 shares of common stock, (2) the issuance of 2,287,120 shares of common stock upon the conversion of our convertible promissory notes based on the initial public offering price of $5.00 per share, (3) the issuance of 13,000,000 shares of our common stock that we are selling in this offering and (4) excluding the exercise of any outstanding warrants. The percentage ownership information assumes no exercise of the underwriters' option to purchase additional shares. Beneficial ownership of shares and percentage ownership are determined in accordance with the rules of the SEC. In calculating the number of shares beneficially owned by an individual or entity and the percentage ownership of that individual or entity, shares underlying options or warrants held by that individual or entity that are either exercisable on March 1, 2015 or exercisable within 60 days from March 1, 2015 are deemed outstanding. These shares, however, are not deemed outstanding for the purpose of computing the percentage ownership of any other individual or entity. Unless otherwise indicated and subject to community property laws where applicable, the individuals and entities named in the table below have sole voting and investment power with respect to all shares of our common stock shown as beneficially owned by them.

Name of Beneficial Owner	Shares Beneficially Owned Before Offering		Shares Beneficially Owned After Offering	
	Number	Percentage	Number	Percentage
5% or Greater Stockholders:				
ACP IV, L.P.(1)	2,708,713	30.2%	4,343,549	17.9%
InterWest Partners IX, L.P.(2)	2,976,881	33.2%	4,619,195	19.0%
Entities affiliated with Vivo Ventures(3)	2,494,592	27.8%	4,204,562	17.3%
Directors and Named Executive Officers:				
David M. Renzi(4)	241,003	2.6%	241,003	1.0%
T. Michael White(5)	—	*	—	*
Hayley Lewis(6)	—	*	—	*
Steven L. Basta(7)	28,001	*	28,001	*
Keith A. Katkin(8)	3,004	*	3,004	*
Edward W. Unkart(9)	3,004	*	3,004	*
David M. Clapper(10)	3,004	*	3,004	*
Albert Cha, M.D., Ph.D.(11)	2,494,592	27.8%	4,204,562	17.3%
Guy P. Nohra(12)	2,708,713	30.2%	4,343,549	17.9%
Reza Zadno, Ph.D.(13)	—	*	—	*
All executive officers and directors as a group(14) (12 persons)	5,722,760	60.3%	9,067,566	36.6%

* Represents beneficial ownership of less than one percent.

(1) Consists of (i) 727,590 shares of common stock issuable upon conversion of shares of Series A preferred stock and (ii) 1,981,123 shares of common stock issuable upon conversion of shares of Series B preferred stock. Shares beneficially owned after this offering also include 757,336 shares of common stock issuable upon conversion of convertible promissory notes held by ACP IV, L.P. and 877,500 shares allocated in this offering. ACP IV, L.P. is a Delaware limited partnership, whose general partner is ACMP IV, LLC, a Delaware limited liability company. Mr. Nohra is a director of ACMP IV, LLC and he exercises shared voting and investment power with the other directors of ACMP IV, LLC with respect to the securities held by ACP IV, L.P. Each director of ACMP IV, LLC disclaims beneficial ownership of such securities, except to the extent of their pecuniary interest therein. The address for ACP IV, L.P. is One Embarcadero Center, Suite 3700, San Francisco, CA 94111.

(2) Consists of (i) 831,531 shares of common stock issuable upon conversion of shares of Series A preferred stock and (ii) 2,145,350 shares of common stock issuable upon conversion of shares of Series B preferred stock. Shares beneficially owned after this offering also include 832,314 shares of common stock issuable upon conversion of convertible promissory notes held by InterWest Partners IX, L.P. and 810,000 shares allocated in this offering. InterWest Partners IX, L.P. is a California limited partnership, whose general partner is InterWest Management Partners IX, LLC. Each managing director and venture member of InterWest Management Partners IX, LLC shares voting and investment power with respect to the securities held by InterWest Partners IX, L.P. and disclaims beneficial ownership of such shares except to the extent of his or her pecuniary interest therein. The address for InterWest Partners IX, L.P. is 2710 Sand Hill Road, Second Floor, Menlo Park, CA 94025.

(3) Consists of (i) 2,476,452 shares of common stock issuable upon conversion of shares of Series B preferred stock held in the name of Vivo Ventures Fund VI, L.P. and (ii) 18,140 shares of common stock issuable upon conversion of shares of Series B preferred stock held in the name of Vivo Ventures VI Affiliates Fund, L.P. Shares beneficially owned after this offering also include 692,398 and 5,072 shares of common stock issuable upon conversion of convertible promissory notes held by Vivo Ventures Fund VI, L.P. and Vivo Ventures VI Affiliates Fund, L.P., respectively, and 1,012,500 shares allocated in this offering. Vivo Ventures Fund VI, L.P., and Vivo Ventures VI Affiliates Fund, L.P. are Delaware limited partnerships, whose general partner is Vivo Ventures VI, LLC, a Delaware limited liability company. Dr. Cha is a managing member of Vivo Ventures Fund VI, LLC and exercises shared voting and investment power with the other managing members of Vivo Ventures VI, LLC with respect to the securities held by Vivo Ventures VI, L.P. and Vivo Ventures VI Affiliates Fund, L.P. Each managing member of Vivo Ventures VI, LLC hereby disclaims any beneficial ownership of any shares directly held by Vivo Ventures Fund VI, L.P. and Vivo Ventures VI Affiliates Fund, L.P., except to the extent of the pecuniary interest therein. The address Vivo Ventures Fund VI, L.P. and Vivo Ventures VI Affiliates Fund, L.P. is 575 High Street, Suite 201, Palo Alto, California 94301.

(4) Consists of 241,003 shares of common stock issuable upon the exercise of stock options within 60 days of March 1, 2015. Mr. Renzi became our president and chief executive officer on June 3, 2013.

(5) Mr. White became our vice president of finance and chief financial officer on July 7, 2014.

(6) Ms. Lewis became our vice president of regulatory affairs and quality assurance on May 12, 2014.

(7) Consists of 28,001 shares of common stock issuable upon exercise of stock options within 60 days of March 1, 2015.

(8) Consists of 3,004 shares of common stock issuable upon exercise of stock options within 60 days of March 1, 2015. Mr. Katkin became a member of our board of directors on December 4, 2014.

(9) Consists of 3,004 shares of common stock issuable upon exercise of stock options within 60 days of March 1, 2015. Mr. Unkart became a member of our board of directors on December 4, 2014.

(10) Consists of 3,004 shares of common stock issuable upon exercise of stock options within 60 days of March 1, 2015. Mr. Clapper became a member of our board of directors on December 4, 2014.

(11) Consists of the shares held of record by entities affiliated with Vivo Ventures listed in footnote (3) above.

(12) Consists of the shares held of record by ACP IV, L.P. listed in footnote (1) above.

(13) Dr. Zadno, a member of our board of directors, is affiliated with InterWest Partners, but is not a managing director or venture member of InterWest Management Partners IX, LLC, and is therefore not a beneficial owner of the shares held of record by the entities affiliated with InterWest Partners listed in footnote (2) above.

(14) Includes 519,455 shares issuable upon exercise of stock options within 60 days of March 1, 2015 and 1,890,000 shares allocated in this offering.

Description of Capital Stock

The following summary describes our capital stock and the material provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, which will become effective immediately prior to the closing of this offering, of the registration rights agreement to which we and certain of our stockholders are parties, and of the Delaware General Corporation Law. Because the following is only a summary, it does not contain all of the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws and amended and restated registration rights agreement, as amended, copies of which have been filed as exhibits to the registration statement of which this prospectus forms a part.

General

Immediately prior to the closing of this offering, we will file our amended and restated certificate of incorporation that authorizes 100,000,000 shares of common stock, $0.001 par value per share, and 5,000,000 shares of preferred stock, $0.001 par value per share. As of December 31, 2014, there were outstanding:

- 8,959,843 shares of our common stock, on an as-converted basis, held by 43 stockholders of record;
- 124,729 shares of our common stock issuable upon exercise of outstanding warrants; and
- 1,328,873 shares of our common stock issuable upon exercise of outstanding stock options.

In connection with this offering, we have consummated a reverse stock split of our outstanding capital stock at a 1-for-4 ratio.

Common Stock

Voting

Holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, including the election of directors, and do not have cumulative voting rights. Accordingly, the holders of a majority of the shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election.

Dividends

Subject to preferences that may be applicable to any then outstanding preferred stock, the holders of common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds. In addition, pursuant to our loan and security agreement with Silicon Valley Bank, we are prohibited from paying cash dividends without the prior consent of Silicon Valley Bank.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering will be, fully paid and nonassessable.

Preferred Stock

All currently outstanding shares of preferred stock will be automatically converted to common stock immediately prior to the closing of this offering.

Following the closing of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock. The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of us and may adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. It is not possible to state the actual effect of the issuance of any shares of preferred stock on the rights of holders of common stock until the board of directors determines the specific rights attached to that preferred stock.

We have no present plans to issue any shares of preferred stock.

Stock Options

As of December 31, 2014, options to purchase 1,328,873 shares of our common stock at a weighted-average exercise price of $2.54 per share were outstanding.

Warrants

Each of the following warrants were issued to Silicon Valley Bank as part of the debt facilities it has provided to us.

As of December 31, 2014, a single warrant to purchase a total of 20,788 shares of our Series A preferred stock was outstanding with an exercise price of $4.81 per share, which will be converted into a warrant to purchase 20,788 shares of common stock upon the completion of this offering. The warrant is exercisable immediately and will expire in December 2016.

As of December 31, 2014, a warrant to purchase a total of 49,892 shares of our Series B preferred stock was outstanding with an exercise price of $4.81 per share, which will be converted into a warrant to purchase 49,892 shares of common stock upon the completion of this offering. The warrant is exercisable immediately and will expire in October 2021.

As of December 31, 2014, a warrant to purchase a total of 35,340 shares of our Series B preferred stock was outstanding with an exercise price of $4.81 per share, which will be converted into a warrant to purchase 35,340 shares of common stock upon the completion of this offering. The warrant is exercisable immediately and expires in February 2023.

As of December 31, 2014, a warrant to purchase a total of 18,709 shares of our Series B preferred stock was outstanding with an exercise price of $4.81 per share, which will be converted into a warrant to purchase 18,709 shares of common stock upon the completion of this offering. The warrant is exercisable immediately and expires in September 2024. See "Certain Relationships and Related Party Transactions — September 2014 Convertible Note Financing."

Convertible Promissory Notes

On September 29, 2014 and February 19, 2015, we issued convertible promissory notes in an aggregate principal amount of $5.0 million and $4.0 million, respectively. Upon completion of this offering, the convertible promissory notes will automatically convert into a number of shares of our common stock equal to the quotient obtained by dividing the entire principal amount and accrued interest on the convertible promissory notes by 80% of the initial public offering price per share of our common stock.

Registration Rights

Following the closing of this offering, certain holders of our common stock, or their transferees, will be entitled to the registration rights set forth below with respect to registration of the resale of such shares under the Securities Act pursuant to an amended and restated registration rights agreement by and among us and certain of our stockholders.

Demand Registration Rights

At any time beginning 180 days following the closing of this offering, and before December 21, 2017, the holders of at least 20% of the registrable securities, as defined in the amended and restated registration rights agreement, have the right to make up to three demands that we file a registration statement under the Securities Act covering registrable securities with an aggregate offering price to the public of not less than $10,000,000, subject to specified exceptions.

Form S-3 Registration Rights

If we are eligible to file a registration statement on Form S-3, holders of registrable securities have the right to two demands in any 12-month period that we file a registration statement on Form S-3 so long as the aggregate amount of securities to be sold under the registration statement on Form S-3 is at least $1.0 million, subject to specified exceptions, conditions and limitations.

"Piggyback" Registration Rights

If we register any securities for public sale, subject to certain exceptions, holders of registration rights will have the right to include their shares in the registration statement. The underwriters of any underwritten offering will have the right to limit the number of shares having registration rights to be included in the registration statement, but not below 20% of the total number of shares requested by the holders to be included in the registration statement, except this offering in which the aggregate amount of registrable securities, if any, may be reduced to zero.

Expenses of Registration

Generally, we are required to bear all registration and selling expenses incurred in connection with the demand, piggyback and Form S-3 registrations described above, other than underwriting discounts and commissions.

Expiration of Registration Rights

All registration rights discussed above will terminate no later than seven years following the closing of this offering, when there are no longer any registrable securities outstanding or, as to a given holder of registrable securities, when such holder is able to sell all of their registrable securities in a single 90-day period under Rule 144 of the Securities Act, or Rule 144.

Anti-Takeover Effects of Provisions of Our Amended and Restated Certificate of Incorporation, Our Bylaws and Delaware Law

Delaware Anti-Takeover Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; upon closing of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Our certificate of incorporation and bylaws will contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of the company unless such takeover or change in control is approved by the board of directors.

These provisions include:

Classified Board. Our certificate of incorporation will provide that our board of directors will be divided into three classes of directors, with the classes as nearly equal in number as possible. As a result, approximately one-third of our board of directors will be elected each year. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of our board. Our bylaws will also provide that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of directors will be fixed exclusively pursuant to a resolution adopted by our board of directors.

Action by Written Consent; Special Meetings of Stockholders. Our certificate of incorporation will provide that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our bylaws will also provide that, subject to any special rights of the holders of any series of preferred stock, and to the requirements of applicable law, special meetings of the stockholders can be called only by or at the direction of the board of directors pursuant to a resolution adopted by a majority of the total number of directors which our board of directors would have if there were no vacancies. Except as described above, stockholders will not be permitted to call a special meeting or to require the board of directors to call a special meeting.

Removal of Directors. Our bylaws will provide that our directors may be removed only for cause by the affirmative vote of at least 66 2/3% of the voting power of our voting stock, voting together as a single class. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board.

Advance Notice Procedures. Our bylaws will establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting will only be able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting. Although the bylaws will not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Super Majority Approval Requirements. The Delaware General Corporation Law generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless either a corporation's certificate of incorporation or bylaws requires a greater percentage. Our certificate of incorporation and bylaws will provide that the affirmative vote of holders of at least 66 2/3% of the total votes eligible to be cast in the election of directors will be required to amend, alter, change or repeal certain provisions of the certificate of incorporation and bylaws. This requirement of a supermajority vote to approve amendments to certain provisions of our certificate of incorporation and bylaws could enable a minority of our stockholders to exercise veto power over any such amendments.

Authorized but Unissued Shares. Our authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital, corporate acquisitions and employee benefit plans. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Forum. Our certificate of incorporation will provide that, to the fullest extent permitted by applicable law, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or (iv) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our certificate of incorporation described above. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable.

Nasdaq Global Market Listing

Our common stock has been approved for listing on The NASDAQ Global Market under the symbol "CBYL."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 620 15th Avenue, Brooklyn, New York 11219.

Shares Eligible For Future Sale

Immediately prior to this offering, there has been no public market for our common stock. Future sales of substantial amounts of common stock in the public market could adversely affect prevailing market prices. Furthermore, since only a limited number of shares will be available for sale shortly after this offering because of contractual and legal restrictions on resale described below, sales of substantial amounts of common stock in the public market after the restrictions lapse could adversely affect the prevailing market price for our common stock as well as our ability to raise equity capital in the future.

Based on the number of shares of common stock outstanding as of December 31, 2014, upon the closing of this offering, 24,246,963 shares of common stock will be outstanding, assuming no exercise of the underwriters' option to purchase additional shares of common stock and no exercise of options. All of the shares sold in this offering will be freely tradable unless held by an affiliate of ours. Except as set forth below, the remaining 11,246,963 shares of common stock outstanding after this offering will be restricted as a result of securities laws or lock-up agreements. These remaining shares will generally become available for sale in the public market as follows:

- No restricted shares will be eligible for immediate sale upon the closing of this offering;
- Up to 11,246,963 restricted shares will be eligible for sale under Rule 144 or Rule 701 of the Securities Act upon expiration of lock-up agreements at least 180 days after the date of this offering; and
- The remainder of the restricted shares will be eligible for sale from time to time thereafter upon expiration of their respective holding periods under Rule 144, as described below, but could be sold earlier if the holders exercise any available registration rights.

Rule 144

In general, under Rule 144 as currently in effect, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, any person who is not an affiliate of ours and has held their shares for at least six months, including the holding period of any prior owner other than one of our affiliates, may sell shares without restriction, provided current public information about us is available. In addition, under Rule 144, any person who is not an affiliate of ours and has held their shares for at least one year, including the holding period of any prior owner other than one of our affiliates, would be entitled to sell an unlimited number of shares immediately upon the closing of this offering without regard to whether current public information about us is available. Beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours and who has beneficially owned restricted securities for at least six months, including the holding period of any prior owner other than one of our affiliates, is entitled to sell a number of restricted shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 242,469 shares immediately after this offering (calculated as of December 31, 2014, on the basis of the assumptions described above and assuming no exercise of the underwriter's option to purchase additional shares and no exercise of outstanding options); or
- the average weekly trading volume of our common stock on The NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 pursuant to Rule 144 with respect to the sale.

Sales of restricted shares under Rule 144 held by our affiliates are also subject to requirements regarding the manner of sale, notice and the availability of current public information about U.S. Rule 144 also provides that affiliates relying on Rule 144 to sell shares of our common stock that are not restricted shares must nonetheless comply with the same restrictions applicable to restricted shares, other than the holding period requirement.

Notwithstanding the availability of Rule 144, the holders of substantially all of our restricted shares have entered into lock-up agreements as described below and their restricted shares will become eligible for sale at the expiration of the restrictions set forth in those agreements.

Rule 701

Under Rule 701 of the Securities Act, or Rule 701, shares of our common stock acquired upon the exercise of currently outstanding options or pursuant to other rights granted under our stock plans may be resold by:

- persons other than affiliates, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, subject only to the manner-of-sale provisions of Rule 144; and
- our affiliates, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, subject to the manner-of-sale and volume limitations, current public information and filing requirements of Rule 144, in each case, without compliance with the six-month holding period requirement of Rule 144.

As of December 31, 2014, options to purchase a total of 1,328,873 shares of common stock were outstanding, of which 549,936 were vested. Of the total number of shares of our common stock issuable under these options, substantially all are subject to contractual lock-up agreements with us or the underwriters described below under “Underwriting” and will become eligible for sale at the expiration of those agreements unless held by an affiliate of ours.

Lock-Up Agreements

We, along with our directors, executive officers and all of our other stockholders and optionholders, have agreed that for a period of 180 days after the date of this prospectus, subject to specified exceptions, we or they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock. Upon expiration of the “lock-up” period, certain of our stockholders will have the right to require us to register their shares under the Securities Act. See “Registration Rights” below.

Registration Rights

Upon the completion of this offering, the holders of an aggregate of 8,268,531 shares of common stock or their permitted transferees, including shares of common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock (excluding exercise of outstanding warrants), will be entitled to rights with respect to the registration of these shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration statement. See “Description of Capital Stock — Registration Rights” for additional information.

Stock Plans

We intend to file with the SEC a registration statement under the Securities Act covering the shares of common stock that we may issue upon exercise of certain outstanding options granted under our 2004 Plan, 2014 Plan and 2015 Equity Plan. Such registration statement is expected to be filed and become effective as soon as practicable after the closing of this offering. Accordingly, shares registered under such registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

Material U.S. Federal Income Tax Consequences to Non-U.S. Holders of Our Common Stock

The following summary describes the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by Non-U.S. Holders (as defined below). This discussion does not address all aspects of U.S. federal income taxes that may be relevant to Non-U.S. Holders in light of their particular circumstances, does not deal with foreign, state, local or estate tax consequences and does not address U.S. federal tax consequences other than income taxes. Special rules different from those described below may apply to certain Non-U.S. Holders that are subject to special treatment under the Internal Revenue Code of 1986, as amended, or the Code, such as financial institutions, insurance companies, persons subject to the alternative minimum tax, tax-exempt organizations, broker-dealers and traders in securities, U.S. expatriates or former citizens or long-term residents of the United States, "controlled foreign corporations," "passive foreign investment companies," corporations that accumulate earnings to avoid U.S. federal income tax, persons that own, or are deemed to own, more than five percent of our capital stock, persons that hold our common stock as part of a "straddle," "hedge," "conversion transaction," "synthetic security" or integrated investment or other risk reduction strategy, persons deemed to sell our common stock under the constructive sale provisions of the Code, tax-qualified retirement plans, partnerships and other pass-through entities, and investors in such pass-through entities or an entity that is treated as a disregarded entity for U.S. federal income tax purposes (regardless of its place of organization or formation). Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local, estate and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code, and U.S. Department of the Treasury, or Treasury, regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income tax consequences different from those discussed below. We have not requested a ruling from the U.S. Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. This discussion assumes that the Non-U.S. Holder holds our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment).

If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

Persons considering the purchase of our common stock pursuant to this offering should consult their own tax advisors concerning the U.S. federal income and any other tax consequences of acquiring, owning and disposing of our common stock in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or foreign tax consequences.

For the purposes of this discussion, a "Non-U.S. Holder" is, for U.S. federal income tax purposes, a beneficial owner of our common stock that has not been excluded from this discussion and is not a U.S. Holder. A "U.S. Holder" means a beneficial owner of our common stock that is for U.S. federal income tax purposes (a) an individual who is a citizen or resident of the United States, (b) a corporation or other entity treated as a corporation created or organized in or under the laws of the United States, any state thereof or the District of Columbia, (c) an estate the income of which is includable in gross income for U.S. federal income tax purposes regardless of its source, or (d) a trust if it (1) is subject to the primary supervision of a court within the United States and one or more "U.S. persons" (within the meaning of Section 7701(a)(30) of the Code) have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable Treasury regulations to be treated as a U.S. person.

Distributions

Subject to the discussion below, distributions, if any, made on our common stock to a Non-U.S. Holder of our common stock to the extent made out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles) generally will constitute dividends for U.S. tax purposes and will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide us with a properly executed IRS Form W-8BEN or W-8BEN-E, or other appropriate form, certifying the Non-U.S. Holder's entitlement to benefits under that treaty. If you are eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, you should consult with your own tax advisor to determine if you are able to obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that such holder maintains in the United States) if a properly executed IRS Form W-8ECI, or other appropriate form, stating that the dividends are so connected, is furnished to us (or, if stock is held through a financial institution or other agent, to such agent). In general, such effectively connected dividends will be subject to U.S. federal income tax, on a net income basis at the regular graduated rates, unless a specific treaty exemption applies. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional "branch profits tax," which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder's effectively connected earnings and profits, subject to certain adjustments. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will constitute a non-taxable return of capital to the extent of your adjusted basis and will first reduce your adjusted basis in our common stock, but not below zero, and then will be treated as gain and taxed in the same manner as gain realized from a sale or other disposition of common stock as described in the next section.

Gain on Disposition of Our Common Stock

Subject to the discussion below regarding backup withholding and foreign accounts, a Non-U.S. Holder generally will not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (a) the gain is effectively connected with a trade or business of such Non-U.S. Holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that such holder maintains in the United States), (b) the Non-U.S. Holder is a non-resident alien individual and is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met, or (c) we are or have been a "United States real property holding corporation" within the meaning of Section 897(c)(2) of the Code at any time within the shorter of the five-year period ending on the date of such disposition or such holder's holding period. In general, we would be a United States real property holding corporation if interests in U.S. real estate comprised (by fair market value) at least half of our business assets (which include U.S. real property interests). We believe that we are not, and do not anticipate becoming, a United States real property holding corporation. Even if we are treated as a United States real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned, directly, indirectly and constructively, no more than 5% of our common stock at all times within the shorter of (i) the five-year period ending on the date of the disposition or (ii) the holder's holding period, and (2) our common stock is regularly traded on an established securities market. We do not make any assurances that our common stock will qualify or continue to qualify as regularly traded on an established securities market.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at regular graduated U.S. federal income tax rates, unless a specific treaty exemption applies, and corporate Non-U.S. Holders described in (a) above may be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (b) above, you will be required to pay a flat 30% tax on the gain derived from the sale, which gain may be offset by U.S. source capital losses (even though you are not considered a resident of the United States).

Information Reporting Requirements and Backup Withholding

Generally, we or certain financial middlemen must report information to the IRS with respect to any dividends we pay on our common stock including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient's country of residence.

Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN, W-8BEN-E, W-8ECI, or W-8EXP, or otherwise establishes an exemption. The backup withholding rate is 28%.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding requirements generally will apply to the proceeds from a disposition of our common stock effected by or through a U.S. office of any broker, U.S. or foreign, except that information reporting and such requirements may be avoided if the holder provides a properly executed IRS Form W-8BEN, W-8BEN-E, W-8ECI, or W-8EXP, or otherwise meets documentary evidence requirements for establishing Non-U.S. Holder status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS. If backup withholding is applied to you, you should consult with your own tax advisor to determine if you are able to obtain a tax benefit or credit with respect to such backup withholding.

Foreign Accounts

Withholding taxes are imposed on certain types of payments made to a foreign financial institution or a non-financial foreign entity (as specifically defined for this purpose), including when the foreign financial institution holds our common stock on behalf of a non-U.S. Holder, unless additional certification, information reporting and other specified requirements are satisfied. The failure of a foreign financial institution or non-financial foreign entity to comply with the reporting requirements could result in a 30% withholding tax being imposed on certain "Withholdable Payments" paid to such entity. For this purpose, subject to certain exceptions, the term "Withholdable Payment" generally includes payment of dividends if such payment is from sources within the United States, as well as any gross proceeds from the sale or other disposition of any property of a type which can produce, among other things, dividends from sources within the United States. If a Non-U.S. Holder does not provide the withholding agent with the information necessary for it to comply with this legislation, it is possible that payments of dividends as well as payments received from sales proceeds to such Non-U.S. Holder will be subject to the 30% withholding tax. Under the applicable Treasury Regulations, such withholding obligations

will generally apply to payments made after September 30, 2014 (in the case of dividends) and to payments made after December 31, 2016 (in the case of certain sales proceeds). Under certain circumstances, a Non-U.S. Holder might be eligible for refunds or credits of such taxes. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. Holders are encouraged to consult with their own tax advisors regarding the possible implications of the legislation on their investment in our common stock.

EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW.

Underwriting

Leerink Partners LLC is acting as the representative of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
Leerink Partners LLC	6,500,000
JMP Securities LLC	3,250,000
Wedbush Securities Inc.	3,250,000
Total	13,000,000

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representative has advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover of this prospectus and to dealers at that price less a concession not in excess of $0.21 per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discounts and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares of our common stock.

	Per Share	Without Option	With Option
Public offering price	$5.00	$ 65,000,000	$ 74,750,000
Underwriting discounts	$0.35	$ 4,550,000	$ 5,232,500
Proceeds, before expenses, to us	$4.65	$ 60,450,000	$ 69,517,500

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $3.4 million. We also have agreed to reimburse the underwriters for up to $40,000 for certain of their expenses, including their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to 1,950,000 additional shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We, our executive officers, directors and certain of our other existing security holders have agreed, subject to certain exceptions, not to sell or transfer any common stock or securities convertible into or exchangeable or exercisable for common stock, for 180 days after the date of this prospectus without first obtaining the written consent of Leerink Partners LLC. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any common stock;
- sell any option or contract to purchase any common stock;
- purchase any option or contract to sell any common stock;
- grant any option, right or warrant for the sale of any common stock;
- otherwise dispose of or transfer any common stock;
- request or demand that we file a registration statement related to the common stock; or
- enter into any swap or other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of any common stock, whether any such swap, agreement or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

The restrictions described in the preceding paragraphs do not apply to:

- transfers or dispositions of shares of common stock (or any security convertible into or exercisable or exchangeable for common stock):
    - as a bona fide gift;
    - to the immediate family of or any trust for the direct or indirect benefit of the person subject to the lock-up restrictions;
    - if the person subject to the lock-up restriction is an entity, as a distribution to the limited partners, members, stockholders or other equity holders of the such entity or as a part of a disposition, transfer or distribution without consideration by such entity to its equity holders;
    - to the undersigned's affiliates or to any investment fund or other entity controlled or managed by the undersigned;

- by operation of law, including pursuant to a qualified domestic order or in connection with a divorce settlement;
- by will or intestate succession upon the death of the undersigned; or

  provided that in the case of any transfer or distribution pursuant to the above subclauses, (i) each donee or distributee shall sign and deliver a lock-up letter substantially in the form executed by the party subject to the lock up restrictions, (ii) such transfer shall not involve a disposition for value, (iii) no filing under Section 16(a)of the Exchange Act, reporting a reduction in beneficial ownership of shares of common stock, shall be required or shall be voluntarily made during the restricted period (except than with respect to transfers by operation of law or by will or intestate succession) and (iv) the person subject to the lock-up restriction does not voluntarily effect and public filing or report;

- sales or transfers to the underwriters in the this offering;
- transfers to the company upon a vesting event of the company's securities or to the company upon the exercise or conversion of options or warrants to purchase the company's securities, in each case, on a "cashless" or "net exercise" basis or to cover tax withholding obligations of the undersigned in connection with such vesting or exercise;
- the conversion of shares of preferred stock of the company into shares of common stock;
- transfers to the company pursuant to agreements under which the company has the option to repurchase or the company has a right of first refusal;
- transfers pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction involving a change in control of the company;
- sales of shares of common stock acquired in open market transactions after the completion of the offering of the shares, *provided* such sales are not required during the 180-day period to be reported in any press release or public report or filing with SEC, or otherwise and the person subject to the lock-up restriction does not otherwise voluntarily effect any press release, public filing or report regarding such sales during the 180-day period; or
- exercises of any rights to purchase, exchange or convert any stock options granted pursuant to our equity incentive plans or warrants or any other securities existing as of the date of this prospectus, which securities are convertible into or exchangeable or exercisable for common stock, if and only if (but subject to any transfers made in connection with "cashless" or "net exercise" transactions described above) the shares of common stock received upon such exercise, purchase, exchange or conversion shall remain subject to the terms of the lock-up agreement.

NASDAQ Global Market Listing

Our common stock has been approved for listing on The NASDAQ Global Market under the symbol "CBYL."

Before this offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations between us and the representative. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price are:

- the valuation multiples of publicly traded companies that the representative believes to be comparable to us;
- our financial information;

- the history of, and the prospects for, our company and the industry in which we compete;
- an assessment of our management, its past and present operations, and the prospects for, and timing of, our future revenues;
- the present state of our development; and
- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the shares may not develop. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

The underwriters do not expect to sell more than 5% of the shares in the aggregate to accounts over which they exercise discretionary authority.

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representative may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. “Covered” short sales are sales made in an amount not greater than the underwriters’ option described above. The underwriters may close out any covered short position by either exercising their option or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. “Naked” short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the closing of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representative has repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on The NASDAQ Global Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representative will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They may in the future receive customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers.

Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant Member State"), no offer of shares may be made to the public in that Relevant Member State other than:

A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;

B. to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representative; or

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require the Company or the representative to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representative has been obtained to each such proposed offer or resale.

The company, the representative and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression "an offer to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Legal Matters

The validity of the issuance of the shares of common stock being offered by this prospectus will be passed upon for us by Ropes & Gray LLP. The underwriters are being represented by Latham & Watkins LLP in connection with this offering.

Experts

The financial statements as of December 31, 2013 and 2014 and for each of the three years in the period ended December 31, 2014 included in this prospectus have been so included in reliance on the report, which contains an explanatory paragraph relating to the Company's ability to continue as a going concern as described in Note 1 to the financial statements, of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

Where You Can Find Additional Information

We have filed with the SEC a registration statement on Form S-1 under the Securities Act, with respect to the shares of common stock being offered by this prospectus. This prospectus does not contain all of the information in the registration statement and its exhibits. For further information with respect to us and the common stock offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract, agreement or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at www.sec.gov. You may also read and copy any document we file with the SEC at its public reference facilities at 100 F Street NE, Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities. You may also request a copy of these filings, at no cost, by writing us at 3181 Porter Drive, Palo Alto, CA 94304 or telephoning us at (650) 855-6777.

Upon the closing of this offering, we will be subject to the information reporting requirements of the Exchange Act, and we will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information will be available for inspection and copying at the public reference room and web site of the SEC referred to above. We also maintain a website at www.carbylan.com, at which, following the closing of this offering, you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is incorporated by reference in, and is not part of, this prospectus.

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Carbylan Therapeutics, Inc.

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Report of Independent Registered Public Accounting Firm

To Board of Directors and Stockholders of Carbylan Therapeutics, Inc:

In our opinion, the accompanying balance sheets and the related statements of operations and comprehensive loss, of convertible preferred stock and stockholders' deficit and of cash flows present fairly, in all material respects, the financial position of Carbylan Therapeutics, Inc. at December 31, 2014 and 2013, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2014 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has a net capital deficiency that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/ PricewaterhouseCoopers LLP

San Jose, California
April 6, 2015

Carbylan Therapeutics, Inc.

Balance Sheets
(in thousands, except share and per share amounts)

	December 31,		Pro Forma December 31, 2014 (Note 2) (unaudited)
	2013	2014	
Assets			
Current assets:			
Cash and cash equivalents	$ 9,781	$ 3,897	
Prepaid expenses and other current assets	129	690	
Total current assets	9,910	4,587	
Property and equipment, net	75	180	
Restricted cash	50	50	
Deferred financing costs	—	1,648	
Other assets	70	179	
Total assets	$ 10,105	$ 6,644	
Liabilities, convertible preferred stock and stockholders' deficit			
Current liabilities:			
Accounts payable	$ 462	$ 1,024	
Accrued expenses	396	1,605	
Loans payable	3,063	4,435	
Deferred licensing revenue	29	29	
Total current liabilities	3,950	7,093	
Convertible promissory notes	—	2,131	—
Derivative liability	—	1,495	—
Preferred stock warrant liability	184	463	—
Deferred licensing revenue, net of current portion	114	85	
Deferred rent, net of current portion	9	2	
Total liabilities	4,257	11,269	
Commitments and contingencies (Note 4)			
Convertible preferred stock, $.001 par value; 34,371,305 shares authorized, 8,268,531 shares issued and outstanding as of December 31, 2013 and 8,268,531 issued and outstanding at December 31, 2014	39,556	39,556	—
Stockholders' deficit:			
Common stock, $.001 par value; 45,000,000 authorized; 442,488 issued and outstanding at December 31, 2013, 691,312 shares issued and outstanding as of December 31, 2014 and 10,225,937 (unaudited) shares outstanding, pro forma	—	1	$ 10
Additional paid-in-capital	708	3,593	49,734
Accumulated deficit	(34,416)	(47,775)	(50,280)
Total stockholders' deficit	(33,708)	(44,181)	$ (536)
Total liabilities, convertible preferred stock and stockholders' deficit	$ 10,105	$ 6,644	

The accompanying notes are an integral part of these financial statements.

Carbylan Therapeutics, Inc.

Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Year Ended December 31,		
	2012	2013	2014
License revenue	$ 1,538	$ 415	$ 29
Operating expenses:			
Research and development	1,959	4,229	8,294
General and administrative	1,412	1,402	3,412
Total operating expenses	3,371	5,631	11,706
Loss from operations	(1,833)	(5,216)	(11,677)
Other income (expense), net:			
Interest income	1	2	2
Interest expense	(256)	(405)	(1,082)
Other income (expense), net	35	(59)	(602)
Total other income (expense), net	(220)	(462)	(1,682)
Net loss and comprehensive loss	$ (2,053)	$ (5,678)	$ (13,359)
Deemed dividend (Note 7)	(111)	—	—
Net loss attributable to common shareholders	$ (2,164)	$ (5,678)	$ (13,359)
Net loss per share attributable to common stockholders, basic and diluted	$ (5.14)	$ (13.42)	$ (21.81)
Weighted average common shares outstanding, basic and diluted	421,152	423,059	612,525
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)			$ (1.46)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)			10,147,150

The accompanying notes are an integral part of these financial statements.

Carbylan Therapeutics, Inc.

Statements of Changes in Convertible Preferred Stock and Stockholders' Deficit
(in thousands, except share and per share amounts)

	Series A and B Convertible Preferred Stock		Common Stock		Additional Paid-in-Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount			
Balance as of January 1, 2012	5,234,275	$ 27,482	421,152	$ —	$ 517	$ (26,685)	$ (26,168)
Issuance of Series B convertible preferred stock at $4.8104, net of issuance costs of $47	1,247,292	5,953	—	—	—	—	—
Issuance of Series B convertible preferred stock and resulting deemed dividend in connection with the modification of Series B convertible preferred stock liquidation preference	534,470	111	—	—	(111)	—	(111)
Stock-based compensation expense			—	—	47	—	47
Net loss			—	—	—	(2,053)	(2,053)
Balance at December 31, 2012	7,016,037	33,546	421,152	—	453	(28,738)	(28,285)
Exercise of stock options			21,254	—	17	—	17
Issuance of Series B convertible preferred stock at $4.8104, net of issuance costs of $14	1,252,494	6,010	—	—	—	—	—
Stock-based compensation expense			—	—	238	—	238
Net loss			—	—	—	(5,678)	(5,678)
Balance at December 31, 2013	8,268,531	39,556	442,406	—	708	(34,416)	(33,708)
Exercise of stock options			248,906	1	228	—	229
Stock-based compensation expense			—	—	381	—	381
Beneficial conversion feature of convertible promissory notes			—	—	2,276	—	2,276
Net loss			—	—	—	(13,359)	(13,359)
Balance at December 31, 2014	8,268,531	$ 39,556	691,312	$ 1	$ 3,593	$ (47,775)	$ (44,181)

The accompanying notes are an integral part of these financial statements.

Carbylan Therapeutics, Inc.

Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2012	2013	2014
Cash flows from operating activities			
Net loss	$(2,053)	$(5,678)	$(13,359)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	38	27	54
Stock based compensation expense	47	238	381
Change in fair value of preferred stock warrant liability and derivative liability	(6)	63	605
Non-cash interest expense	104	32	64
Amortization of convertible promissory notes discount	—	—	384
Changes in operating assets and liabilities:			
Prepaid expenses and other current asset	1	(46)	(561)
Other assets	(38)	—	(109)
Accounts payable	(8)	315	487
Accruals	(64)	183	837
Deferred licensing revenue	137	6	(29)
Deferred rent	7	2	(7)
Net cash used in operating activities	(1,835)	(4,858)	(11,253)
Cash flows from investing activities			
Purchase of property and equipment	(91)	(18)	(159)
Net cash used in investing activities	(91)	(18)	(159)
Cash flows from financing activities			
Proceeds from issuance of common stock, net	—	17	229
Proceeds from issuance of convertible preferred stock, net	5,953	6,010	—
Deferred public offering costs	—	—	(1,201)
Proceeds from loans payable	—	546	2,208
Proceeds from convertible promissory notes	—	—	5,000
Repayment of loans payable	(389)	(158)	(708)
Net cash provided by financing activities	5,564	6,415	5,528
Net increase (decrease) in cash and cash equivalent	3,638	1,539	(5,884)
Cash and cash equivalents at beginning of period	4,604	8,242	9,781
Cash and cash equivalents at end of period	$ 8,242	$ 9,781	$ 3,897
Supplemental cash flow information			
Cash paid for interest	$ 152	$ 367	$ 626
Supplemental disclosure of non-cash financing activities			
Issuance of preferred stock warrants	18	42	103
Deemed dividend on preferred stock	111	—	—
Deferred public offering costs	—	—	447
Derivative related to convertible promissory notes upon issuance	—	—	1,067
Beneficial conversion feature of convertible promissory notes	—	—	2,275

The accompanying notes are an integral part of these financial statements.

Carbylan Therapeutics, Inc.

Notes to Financial Statements

1. Organization and Basis of Presentation

Carbylan Therapeutics, Inc. (the "Company") is a clinical-stage specialty pharmaceutical company focused on the development and commercialization of novel and proprietary combination therapies that address significant unmet medical needs. The Company's initial focus is on the development of Hydros-TA, its proprietary, potentially best-in-class intra-articular injectable product candidate to treat pain associated with osteoarthritis of the knee. The Company was incorporated in the state of Delaware on March 26, 2004 as Sentrx Surgical, Inc. The name of the Company was changed to Carbylan Biosurgery, Inc. on December 14, 2005. The name of the Company was changed to Carbylan Therapeutics, Inc. on March 7, 2014.

Since commencing operations in 2004, the Company has devoted substantially all of its efforts to identifying and developing product candidates for therapeutic markets, recruiting personnel and raising capital. The Company has devoted predominantly all of its resources to the preclinical and clinical development of, and manufacturing capabilities for, Hydros-TA. The Company has never been profitable and has not yet commenced commercial operations.

The financial statements have been prepared on a going-concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. In order to continue its operations, the Company must raise additional equity or debt financings and achieve profitable operations. Although management has been successful in raising capital in the past, there can be no assurance that the Company will be able to obtain additional equity or debt financing on terms acceptable to the Company, or at all. The failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company's business, results of operations, future cash flows and financial condition. As a company with no commercial operating history, the Company is subject to all of the risks and expenses associated with a start-up company. The Company must among other things respond to competitive developments, attract, retain and motivate qualified personnel and support the expense of marketing new products based on innovative technology. The Company has incurred operating losses and negative cash flow from operations in each year since inception. The Company has not generated any revenue from product sales to date and will continue to incur significant research and development and other expenses related to its ongoing operations. The Company has incurred net losses of $2,053,000, $5,678,000, and $13,359,000 for the years ended December 31, 2012, 2013 and 2014, and had an accumulated deficit to December 31, 2014 of $47,775,000. The Company has funded its operations primarily through the sale and issuance of convertible preferred stock and term debt with a financial institution, and convertible promissory notes. As of December 31, 2014, the Company had capital resources consisting of cash and cash equivalents of $3,897,000. These factors raise substantial doubt about the Company's ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP").

Use of Estimates

The preparation of the accompanying financial statements in accordance with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the

Carbylan Therapeutics, Inc.

Notes to Financial Statements

disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting periods. On an ongoing basis, the Company evaluates its estimates, including those related to common stock, stock-based compensation expense, warrant liabilities, accruals, derivative liability, deferred tax valuation allowance and revenue recognition. Management bases its estimates on historical experience or on various other assumptions, including information received from its service providers, which it believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Unaudited Pro Forma Balance Sheet Information

The unaudited pro forma balance sheet information has been prepared assuming immediately prior to the closing of the Company's initial public offering: (i) the automatic conversion of all outstanding shares of convertible preferred stock into shares of common stock, (ii) the conversion of preferred stock warrants into warrants exerciseable for common stock and the related reclassification of the convertible preferred stock warrant liability to common stock and additional paid-in-capital, and (iii) the conversion of the outstanding principal and accrued interest on the September 2014 convertible promissory notes into common stock and the resulting loss on extinguishment of $2.5 million. The unaudited pro forma balance sheet information does not assume any proceeds from the proposed initial public offering.

Risks and Uncertainties

The product candidates developed by the Company require approvals from the U.S. Food and Drug Administration (FDA) or foreign regulatory agencies prior to commercial sales. There can be no assurance that the Company's current and future product candidates will receive the necessary approvals. If the Company is denied approval or approval is delayed, it may have a material adverse impact on the Company's business and its financial statements.

The Company is subject to risks common to companies in the specialty pharmaceutical industry with no commercial operating history, including, but not limited to, dependency on the clinical and commercial success of its product candidates, ability to obtain regulatory approval of its product candidates, the need for substantial additional financing to achieve its goals, uncertainty of broad adoption of its approved products, if any, by physicians and consumers, significant competition and untested manufacturing capabilities.

The Company expects to incur substantial operating losses for the next several years and will need to obtain additional financing in order to launch and commercialize any products or product candidates for which it receives regulatory approval. There can be no assurance that such financing will be available or will be at terms acceptable by the Company.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash and cash equivalents. The Company invests its excess cash in money market accounts. The Company's cash and cash equivalents are held by a single financial institution and all cash is held in the United States. Such deposits may, at times, exceed federally insured limits. The Company has not recognized any losses during the periods presented and management does not believe that the Company is exposed to significant credit risk from its cash and cash equivalents.

Carbylan Therapeutics, Inc.

Notes to Financial Statements

Segment Reporting

The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions. The Company is a specialty pharmaceutical company focused on the development and commercialization of novel and proprietary combination therapies that address significant unmet medical needs. No product revenue has been generated since inception, and all assets are held in the United States.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with an original maturity date of 90 days or less on the date of purchase to be cash equivalents. The Company invests its cash in bank deposits and money market funds.

Restricted Cash

The Company is required to guarantee the credit limit on its corporate credit card with a certificate of deposit of $50,000. The balance is included as restricted cash on the accompanying balance sheets.

Beneficial Conversion Feature

From time to time, the Company may issue convertible notes that have conversion prices that create an embedded beneficial conversion feature on the issuance date. A beneficial conversion feature exists on the date a convertible note is issued when the fair value of the underlying common stock to which the note is convertible into is in excess of the remaining unallocated proceeds of the note after first considering the allocation of a portion of the note proceeds to the fair value of any attached equity instruments, if any related equity instruments were granted with the debt. The intrinsic value of the beneficial conversion feature is recorded as a debt discount with a corresponding amount to additional paid-in capital. The debt discount is amortized to interest expense over the life of the note using the effective interest method.

Embedded Derivatives Related to Convertible Promissory Notes

Embedded derivatives that are required to be bifurcated from the underlying debt instrument (i.e. host) are accounted for and valued as a separate financial instrument. The Company evaluated the terms and features of the convertible promissory notes issued in September 2014 and identified embedded derivatives requiring bifurcation and accounting at fair value because the economic and contractual characteristics of the embedded derivatives met the criteria for bifurcation and separate accounting due to the conversion features (see Note 7 for a description of the conversion features).

Fair Value of Financial Instruments

Fair value accounting is applied for all financial assets and liabilities and non-financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually). As of December 31, 2014, based on borrowing rates that are available to the Company for loans of similar terms and consideration of the Company’s credit risk, the carrying value of the loan payable approximates the fair value using Level 2 inputs.

Carbylan Therapeutics, Inc.

Notes to Financial Statements

Property and Equipment, Net

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, which are as follows:

Computer equipment	3 years
Lab equipment	3 years
Furniture and fixtures	5 years
Machinery and equipment	3 years

Leasehold improvements are amortized over the lesser of their useful lives or the term of the lease. Upon sale or retirement of the assets, the cost and related accumulated depreciation are removed from the balance sheet and the resulting gain or loss is recognized in the accompanying statement of operations and comprehensive loss in other income (expense), net. Maintenance and repairs are charged to operations as incurred.

Pre-clinical and Clinical Trial Accruals

The Company's clinical trial accruals are based on estimates of patient enrollment and related costs at clinical investigator sites as well as estimates for the services received and efforts expended pursuant to contracts with clinical research organizations that conduct and manage preclinical and clinical trials on the Company's behalf. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, the Company modifies the estimates of accrued expenses accordingly. To date, there have been no material differences from its estimates to the amount actually incurred.

Preferred Stock Warrant Liability

The Company accounts for its warrants as either equity or liabilities based upon the characteristics and provisions of each instrument. Warrants classified as derivative liabilities are recorded on the Company's accompanying balance sheets at their fair value on the date of issuance and are revalued at each subsequent balance sheet date, with fair value changes recognized as increases or reductions to other income (expense), net in the statements of operations and comprehensive loss.

Deferred Offering Costs

The Company capitalizes certain legal, accounting and other third-party fees that are directly associated with in-process equity financings as other assets until such financings are consummated. After closing of the equity financing, these costs are recorded in stockholders' deficit as a reduction of additional paid-in-capital generated as a result of the offering. As of December 31, 2014, the Company recorded deferred offering costs of $1,648,000 on the accompanying balance sheet in contemplation of its initial public offering. Should the closing of the initial public offering no longer be considered probable, the deferred offering costs would be expensed immediately as a charge to operating expenses in the accompanying statement of operations and comprehensive loss. The Company did not record any deferred offering costs as of December 31, 2013.

License Revenue

Revenue under the Company's license arrangement is recognized based on the performance requirements of the contract. Determinations of whether persuasive evidence of an arrangement exists and whether delivery has occurred or services have been rendered are based on management's judgments regarding the fixed nature of the

fees charged for deliverables and the collectability of those fees. Should changes in conditions cause management to determine that these criteria are not met for any new or modified transactions, revenue recognized could be adversely affected.

The Company recognizes revenue related to its license arrangement in accordance with the provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605-25, *Revenue Recognition — Multiple-Element Arrangements* ("ASC Topic 605-25,") which provides guidance on how deliverables in an arrangement should be separated and how the arrangement consideration should be allocated to the separate units of accounting:

- requiring an entity to determine the selling price of a separate deliverable using a hierarchy of (i) vendor-specific objective evidence ("VSOE,") (ii) third-party evidence ("TPE,") or (iii) best estimate of selling price ("BESP"); and

- requiring the allocation of the arrangement consideration, at the inception of the arrangement, to the separate units of accounting based on relative fair value.

The Company evaluates all deliverables within an arrangement to determine whether or not they provide value on a stand-alone basis. Based on this evaluation, the deliverables are separated into units of accounting. The arrangement consideration that is fixed or determinable at the inception of the arrangement is allocated to the separate units of accounting based on their relative selling prices. The Company may exercise significant judgment in determining whether a deliverable is a separate unit of accounting, as well as in estimating the selling prices of such unit of accounting.

To determine the selling price of a separate deliverable, the Company uses the hierarchy as prescribed in ASC Topic 605-25 based on VSOE, TPE or BESP. VSOE is based on the price charged when the element is sold separately and is the price actually charged for that deliverable. TPE is determined based on third-party evidence for a similar deliverable when sold separately and BESP is the price at which the Company would transact a sale if the elements of collaboration and license arrangements were sold on a stand-alone basis. The Company may not be able to establish VSOE or TPE for the deliverables within collaboration and license arrangements, as the Company does not have a history of entering into such arrangements or selling the individual deliverables within such arrangements separately. In addition, there may be significant differentiation in these arrangements, which indicates that comparable third-party pricing may not be available. The Company may determine that the selling price for the deliverables within collaboration and license arrangements should be determined using BESP. The process for determining BESP involves significant judgment on the Company's part and includes consideration of multiple factors such as estimated direct expenses and other costs, and available data.

For each unit of accounting identified within an arrangement, the Company determines the period over which the performance obligation occurs. The Company allocates the arrangement consideration to the separate units of accounting based on the relative selling prices. Revenue is recognized immediately if the performance obligation has been met. The Company recognizes the revenue that is deferred using the straight-line method over the expected delivery period of the unit of accounting. Non-substantive regulatory milestone and commercialization royalty payments are recognized in proportion to the two units of accounting identified at the inception of the agreement. Each portion will be recognized in accordance with the underlying unit of accounting. The Company accounts for revenue net of applicable foreign taxes.

Carbylan Therapeutics, Inc.

Notes to Financial Statements

Research and Development Expenditures

Costs incurred to further the Company's research and development include salaries and related employee benefits, stock-based compensation expense, costs associated with clinical studies, nonclinical research and development activities, regulatory activities, research-related overhead expenses and fees paid to external service providers and contract research and manufacturing organizations that conduct certain research and development activities on behalf of the Company.

Income Taxes

The Company accounts for income taxes under the asset and liability method. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amounts expected to be realized.

The Company accounts for uncertain tax positions in accordance with ASC 740-10, *Accounting for Uncertainty in Income Taxes.* The Company assesses all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon ultimate settlement. As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and the Company will determine whether (i) the factors underlying the sustainability assertion have changed and (ii) the amount of the recognized tax benefit is still appropriate. The recognition and measurement of tax benefits requires significant judgment. Judgments concerning the recognition and measurement of a tax benefit might change as new information becomes available.

Stock-Based Compensation

The Company maintains performance incentive plans under which inventive stock options and non-qualified stock options may be granted to employees and non-employees. The Company accounts for stock-based compensation arrangements with employees in accordance with ASC 718, *Compensation — Stock Compensation.* ASC 718 requires the recognition of compensation expense, using a fair value-based method, for costs related to all share-based payments including stock options.

The Company's determination of the fair value of stock options on the date of grant utilizes the Black-Scholes option-pricing model, and is impacted by its common stock price as well as changes in assumptions regarding a number of highly complex and subjective variables. These variables include, but are not limited to, expected term that options will remain outstanding, expected common stock price volatility over the term of the option awards, risk-free interest rates and expected dividends.

The fair value is recognized over the period during which an optionee is required to provide services in exchange for the option award, known as the requisite service period (usually the vesting period), on a straight-line basis. Stock-based compensation expense recognized at fair value includes the impact of estimated forfeitures. The Company estimates future forfeitures at the date of grant and revises the estimates, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Carbylan Therapeutics, Inc.

Notes to Financial Statements

Equity instruments issued to non-employees are recorded at their fair value on the measurement date and are subject to periodic adjustments as the underlying equity instruments vest. The fair value of options granted to consultants is expensed when vested. The non-employee stock-based compensation expense was not material for all periods presented.

Net Loss per Share Attributable to Common Stockholders

The Company calculates its basic and diluted net income (loss) per share attributable to common stockholders in conformity with the two-class method required for companies with participating securities, which are securities other than common stock that are entitled to receive dividends. The Company's convertible preferred stockholders are entitled to participate in dividends and earnings of the Company when dividends are paid on common stock. Under the two-class method, the Company determines whether it has net income attributable to common stockholders, which includes the results of operations, capital contributions and deemed dividends less current period convertible preferred stock non-cumulative dividends. If it is determined that the Company does have net income attributable to common stockholders during a period, the related undistributed earnings are then allocated between common stock and the convertible preferred stock based on the weighted average number of shares outstanding during the period to determine the numerator for the basic net income per share attributable to common stockholders. In computing diluted net income attributable to common stockholders, undistributed earnings are re-allocated to reflect the potential impact of dilutive securities to determine the numerator for the diluted net income per share attributable to common stockholders.

The Company's basic net income (loss) per share attributable to common stockholders is calculated by dividing the net income (loss) by the weighted average number of shares of common stock outstanding for the period. The diluted net income (loss) per share attributable to common stockholders is computed by giving effect to all potential dilutive common stock equivalents outstanding for the period. For purposes of this calculation, options to purchase common stock and common stock warrants are considered common stock equivalents. For periods in which the Company has reported net losses, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. Potential common shares will always be anti-dilutive for periods in which the Company has reported a net loss. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders for the years ended December 31, 2012, 2013 and 2014.

Unaudited Pro Forma Net Loss per Share Attributable to Common Stockholders

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders has been computed to give effect to the automatic conversion immediately prior to the closing of the initial public offering of the convertible preferred stock into common stock as of the beginning of January 1, 2014 or the issuance date, if later, the conversion of all of the Company's warrants exercisable for convertible preferred stock into warrants exercisable for shares of its common stock, and the conversion of its September 2014 convertible promissory notes and 94 days of accrued interest thereon into shares of common stock and the resulting loss on extinguishment of $2.5 million based on the initial public offering price of $5.00 per share. Also, the numerator in the pro forma basic and diluted net loss per share calculation has been adjusted to remove the gains and losses resulting from the re-measurement of the convertible preferred stock warrant liability and derivative liability as these amounts will be reclassified to additional paid-in-capital upon the closing of the initial public offering of the Company's common stock.

Carbylan Therapeutics, Inc.

Notes to Financial Statements

Reverse Stock Split

In March 2015, the Company's board of directors and stockholders approved a 4-for-1 reverse stock split of the Company's common and preferred stock. The Company filed an amendment to its certificate of incorporation effecting the reverse stock split on March 13, 2015.

Recent Accounting Pronouncements

In June 2014, the FASB issued ASU No. 2014-12, *Compensation — Stock Compensation (Topic 718): Accounting for Share-Based Payments When the Terms of an Award Provide That a Performance Target Could be Achieved After a Requisite Service Period* ("ASU 2014-12.") Companies commonly issue share-based payment awards that require a specific performance target to be achieved in order for employees to become eligible to vest in the awards. ASU 2014-12 requires that a performance target that affects vesting and that could be achieved after the requisite service period should be treated as a performance condition. The performance target should not be reflected in estimating the grant date fair value of the award. Compensation cost should be recognized in the period in which it becomes probable that the performance target will be achieved. ASU 2014-12 will be effective for the Company's fiscal years beginning fiscal 2016 and interim reporting periods within that year, using either the retrospective or prospective transition method. Early adoption is permitted. The Company is currently evaluating the effect of the adoption of this guidance on the financial statements.

In June 2014, the FASB issued ASU No. 2014-10, *Development Stage Entities (Topic 915): Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation* ("ASU 2014-10.") ASU 2014-10 removes all incremental financial reporting requirements regarding development-stage entities, including the removal of Topic 915 from the FASB Accounting Standards Codification. In addition, ASU 2014-10 adds an example disclosure in Risks and Uncertainties (Topic 275) to illustrate one way that an entity that has not begun planned operations could provide information about risks and uncertainties related to the company's current activities. ASU 2014-10 also removes an exception provided to development-stage entities in Consolidations (Topic 810) for determining whether an entity is a variable interest entity. ASU 2014-10 will be effective for our fiscal years beginning 2016 and interim reporting period beginning in fiscal 2016. The revisions to Consolidation (Topic 810) are effective for our fiscal years beginning fiscal 2016. Early adoption is permitted. The Company has elected to early adopt this guidance as it relates to all incremental financial reporting requirements regarding development-stage entities.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers Topic 606,* ("ASU 2014-09"). ASU 2014-09 requires entities to recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. ASU 2014-09 requires entities to disclose both qualitative and quantitative information that enables users of financial statements to understand the nature, amount, timing and uncertainty of revenue and cash flows arising from contracts with customers, including disclosure of significant judgments affecting the recognition of revenue. ASU 2014-09 will be effective for the Company's fiscal years beginning 2017 and interim reporting periods within that year, using either the retrospective or cumulative effect transition method. Early adoption is not permitted. The Company is currently evaluating the effect of the adoption of this guidance on the financial statements.

In August 2014, the FASB issued ASU No. 2014-15, ("ASU 2014-15"), *"Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern."* ASU 2014-15 requires management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date the financial statements are issued and provides guidance on determining when and how to disclose going concern

uncertainties in the financial statements. Certain disclosures will be required if conditions give rise to substantial doubt about an entity's ability to continue as a going concern. ASU 2014-15 applies to all entities and is effective for annual and interim reporting periods ending after December 15, 2016, with early adoption permitted. The Company does not expect that the adoption of this guidance will have a material effect on its financial statements.

In November 2014, the FASB issued ASU No. 2014-16 ("ASU 2014-16"), *Derivatives and Hedging (Topic 815): Determining Whether the Host Contract in a Hybrid Financial Instrument Issued in the Form of a Share is More Akin to Debt or to Equity*. ASU 2014-16 was issued to clarify how current U.S. generally accepted accounting principles should be interpreted in evaluating the economic characteristics and risk of a host contract in a hybrid financial instrument that is issued in the form of a share. In addition, ASU 2014-16 was issued to clarify that in evaluating the nature of a host contract, an entity should assess the substance of the relevant terms and features (that is, the relative strength of the debt-like or equity-like terms and features given the facts and circumstances) when considering how to weight those terms and features. The effects of initially adopting ASU 2014-16 should be applied on a modified retrospective basis to existing hybrid financial instruments issued in a form of a share as of the beginning of the fiscal year for which the amendments are effective. Retrospective application is permitted to all relevant prior periods. ASU 2014-16 is effective fiscal years, and interim periods within those fiscal years, beginning after December 15, 2015. Early adoption in an interim period is permitted. The Company is currently evaluating the impact of the adoption of ASU 2014-16 on its financial statements.

Fair Value Measurements

The Company follows ASC 820-10, *Fair Value Measurements and Disclosures*, which among other things, defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or nonrecurring basis. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, a three-tier fair value hierarchy has been established, which prioritizes the inputs used in measuring fair value as follows:

Level 1	Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.
Level 2	Inputs (other than quoted prices included in Level 1) are either directly or indirectly observable for the asset or liability through correlation with market data at the measurement date and for the duration of the instrument's anticipated life.
Level 3	Inputs reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

The Company's investments in money market funds are measured at fair value on a recurring basis. The money market funds comply with Rule 2a-7 of the Investment Company Act of 1940 and are required to be priced and have a fair value of $1.00 net asset value per share. These money market funds are actively traded and reported daily through a variety of sources. Due to the structure and valuation required by the Investment Company Act of 1940 regarding Rule 2a-7 funds, the fair value of the money market fund investments is classified as Level 1.

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The fair value of the certificates of deposit is classified as Level 2 due to the nature of a contractual restriction with a financial institution that requires the certificate of deposit to remain in place as collateral for the credit card, and therefore the ability to liquidate the investment is limited.

There were no transfers between Level 1 and Level 2 during the periods presented.

In certain cases where there is limited activity or less transparency around inputs to valuation, securities are classified as Level 3. Level 3 liabilities that are measured at fair value on a recurring basis consist of the convertible preferred stock warrant liability. In 2012, the Company estimated the fair value of the preferred stock warrant liability by using the backsolve method to determine an enterprise value of the Company. The enterprise value was allocated using the Black-Scholes option-pricing model. In 2013 and 2014, the Company estimated the fair value of the warrant liability by calculating the enterprise value by applying a probability of two scenarios, going public or remaining private. To allocate the enterprise value, the Company used the current value method in the scenario of going public or being acquired. The Company used the Black-Scholes option-pricing method to allocate the enterprise value for the remaining private scenario. Generally, increases or decreases in the fair value of the underlying convertible preferred stock would result in a directionally similar impact in the fair value measurement of the warrant liability.

The fair value of the conversion feature of the September 2014 convertible promissory notes (see Note 7) was recorded as a derivative liability instrument that will be measured at fair value at each reporting period. The Company estimated the fair value of the derivative by estimating the fair value of the convertible promissory notes with and without the conversion derivative. To calculate the fair value of the convertible promissory notes without the conversion derivative, the Company estimated the present value of the expected cash payments at an assumed discount rate of 8.25%. To calculate the fair value of the convertible promissory notes with the conversion feature, the Company calculated the present value of the convertible promissory notes upon conversion at an initial public offering, and the present value of the convertible promissory notes at an equity financing. The risk-free rate for the assumed discount period is estimated at .05% and .15% in the respective conversion scenarios, and the risk-free rate for the assumed discount period is estimated at 0.05% and 0.12% at valuation date of December 31, 2014. The Company applied a probability of occurrence to all of the conversion scenarios and estimated a weighted value of the notes with the conversion feature. The difference between the fair value of the convertible promissory notes with and without the conversion features is the fair value of the derivative. The fair value of the derivative at the date of issuance is $1,067,000, and the fair value of the derivative at December 31, 2014 is $1,495,000.

The following table presents the Company's fair value hierarchy for assets and liabilities measured at fair value on a recurring basis as of December 31, 2013 and 2014:

	Fair Value Measurements as of December 31, 2013 (in thousands)			
	Quoted Price in Active Markets for Identical Assets Level 1	Significant other Observable Inputs Level 2	Significant Unobservable Inputs Level 3	Total
Assets				
Money market funds[1]	$ 9,716	$ —	$ —	$9,716
Certificate of deposit	—	50	—	50
	$ 9,716	$ 50	$ —	$9,766
Liabilities				
Preferred stock warrant liability	$ —	$ —	$ 184	$ 184

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	Fair Value Measurements as of December 31, 2014 (in thousands)			
	Quoted Price in Active Markets for Identical Assets Level 1	Significant other Observable Inputs Level 2	Significant Unobservable Inputs Level 3	Total
Assets				
Money market funds[1]	$ 3,825	$ —	$ —	$3,825
Certificate of deposit	—	50	—	50
	$ 3,825	$ 50	$ —	$3,875
Liabilities				
Derivative liability	$ —	$ —	$ 1,495	$1,495
Preferred stock warrant liability	$ —	$ —	$ 463	$ 463
	$ —	$ —	$ 1,958	$1,958

(1) Included in cash and cash equivalents in the Company's balance sheet.

The change in the fair value of the preferred stock warrant liability is summarized below:

Fair value as of January 1, 2012	$ 67
Fair value of new warrant issued	18
Change in fair value recorded in other income (expense), net	(6)
Fair value as of December 31, 2012	$ 79
Fair value of new warrant issued	42
Change in fair value recorded in other income (expense), net	63
Fair value as of December 31, 2013	$184
Fair value of new warrant issued	103
Change in fair value recorded in other income (expense), net	176
Fair value as of December 31, 2014	$463

The following is a summary of the activity of the derivative liability for the year ended December 31, 2014:

Fair Value at December 31, 2013	$ 0
Embedded derivative liability upon issuance of convertible promissory notes	1,067
Change in fair value recorded in other income (expense), net	428
Fair Value at December 31, 2014	$1,495

The fair value of the derivative liability was determined using the following assumptions (see Note 7):

	At issuance	At December 31, 2014
Discount rate	8.25%	8.25%
Risk-free interest rate for conversion at initial public offering scenario	0.05%	0.05%
Risk-free interest rate for conversion at next series equity financing scenario	0.15%	0.12%

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3. Balance Sheet Components

Property and Equipment, Net

Property and equipment, net, as of December 31, 2013 and 2014 consisted of the following (in thousands):

	December 31, 2013	December 31, 2014
Computer equipment	$ 26	$ 30
Lab equipment	402	543
Furniture and fixtures	21	21
Machinery and equipment	12	26
Leasehold improvement	55	55
	516	675
Less: Accumulated depreciation and amortization	(441)	(495)
Total property and equipment, net	$ 75	$ 180

Depreciation expense for the years ended December 31, 2012, 2013 and 2014, was $38,000, $27,000, and $54,000, respectively.

Accrued Liabilities

(in thousands)

	December 31, 2013	December 31, 2014
Accrued payroll and related expenses	$201	$ 723
Accrued legal expenses	10	159
Accrued research and clinical trial expenses	141	380
Accrued professional services and other	44	343
	$396	$1,605

4. Commitments and Contingencies

Operating Lease

The Company leases its facilities under a noncancelable operating lease which expires in February 2016. The terms of the lease agreement required the Company to provide a security deposit of $69,000. The security deposit is included in other assets on the accompanying balance sheets. The Company has a sub-lease agreement with a tenant for approximately thirty-seven percent of the square footage of the corporate headquarters. Under this agreement, the Company receives $16,000 per month as rental income which is accounted for a reduction of rent expense. The sub-lease agreement continues until February 29, 2016.

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At December 31, 2014, the aggregate future minimum lease payments under this operating lease are as follows:

Years ending December 31,	**(in thousands)**
2015	438
2016	73
Total minimum lease payments	$ 511

Gross rent expense for the years ended December 31, 2012, 2013 and 2014 was $306,000, $413,000 and $429,000, respectively. The rental expense is reduced by the sublease rental income amounts of $75,000, $186,000 and $190,000, respectively, for the same periods.

Indemnification

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for general indemnification. The Company's exposure under these agreements is unknown because it involves future claims that may be made against the Company but have not yet been made. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. However, the Company may record charges in the future as a result of these indemnification obligations.

No amounts associated with such indemnifications have been recorded to date.

Contingencies

From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of business activities. The Company accrues a liability for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. There have been no contingent liabilities requiring accrual or disclosure at December 31, 2012, 2013 and 2014.

5. License Agreement with Shanghai Jingfeng Pharmaceutical Co. Ltd.

In November 2012, the Company entered into a technology license agreement (the "Agreement") with Shanghai Jingfeng Pharmaceutical Co. Ltd. ("Jingfeng"), pursuant to which the Company granted to Jingfeng the exclusive right and license under certain patents to develop, manufacture and commercialize Hydros-TA for human and veterinary uses in China, Taiwan, Hong Kong and Macau. In these countries, Jingfeng is responsible for the manufacture and supply of Hydros-TA, the management and funding of all development activities, regulatory submissions and regulatory approvals for Hydros-TA and the commercialization of Hydros-TA. The Company has also agreed to provide know-how and reasonable professional and technical support services to Jingfeng until Jingfeng performs all efforts necessary to bring the product to commercialization and begins selling the product upon regulatory approval in the aforementioned territory. The Agreement provides for an up-front license payment of $2,000,000 ($1,674,000 net of Chinese withholding taxes), regulatory milestone payments of up to $2,000,000 (excluding Chinese withholding taxes) and future commercial milestone payments of up to approximately $5,000,000 (excluding Chinese withholding taxes) at current exchange rates based on Jingfeng achieving certain gross sales thresholds.

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The Company has identified the following non-contingent performance deliverables at the inception of the Agreement: (i) an exclusive royalty bearing license to certain of the Company's patents relating to Hydros-TA (the "License"), which was transferred immediately upon signing of the Agreement, and (ii) know-how, reasonable professional and technical support services to be provided by the Company to assist Jingfeng in manufacturing, developing and/or commercializing the licensed product (the "Services") throughout the period of the Agreement. The Company has determined that the License represents a separate unit of accounting as the License has standalone value apart from the Services because the development, manufacturing and commercialization rights conveyed would allow Jingfeng to perform all efforts necessary to use the Company's technologies to bring the product to commercialization and begin selling the product upon regulatory approval. Jingfeng can sublicense its rights to the License; and the Services provided by the Company could be performed by a third-party. Therefore, the License and Services represent separate units of accounting.

The Company has determined the BESP for the License unit of accounting using a discounted cash flow analysis. This measurement is based on the value indicated by current estimates of future payments to be received under the agreement and reflects management determined estimates and assumptions. These estimates and assumptions include but are not limited to estimated sales prices, estimated market opportunity, expected market share, the likelihood that clinical trials will be successful, the likelihood that regulatory approval will be received, the likelihood that the products will become commercialized, the determination of the markets served and the discount rate. The Company reduced the future payment to be received by the estimated amount of the professional service costs plus an estimated margin, which was based on industry benchmarking of similar companies. These estimates and assumptions formed the basis of an expected net future cash flow that was discounted based on an estimated weighted average cost of capital. The Company has also determined the BESP for the Services unit of accounting based on the estimated cost of the professional services plus an estimated margin which was based on industry benchmarking of similar companies. These estimates and assumptions formed the basis of an expected net future cash flow that was discounted based on an estimated weighted average cost of capital.

The considerations of the Agreement have been allocated to the units of accounting based on the relative selling price method. Of the $1,674,000 up-front payment received, $1,534,000 was allocated to the License and $140,000 to the Services. The Company has recognized license revenue upon execution of the Agreement as the license has been delivered pursuant to the terms of the Agreement. The $140,000 allocated to Services will be recognized as revenue on a straight-line over the performance period which is currently estimated to be January 2019. The way in which the Company will provide professional services does not give rise to a more precise pattern of recognition and the Company therefore will recognize revenue on a straight-line basis over the performance period.

Of the $421,000 regulatory milestone payment received in November 2013 upon the successful production by Jingfeng of the first batch of Hydros-TA, $385,000 was allocated to the License and $35,000 was allocated to the Services. The Company has recognized license revenue upon execution of the Agreement as the associated unit of accounting had been delivered pursuant to the terms of the Agreement. The $35,000 allocated to Services will be recognized as revenue on a straight-line basis over the performance period which is currently estimated to be January 2019.

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Total revenue recognized with respect to the Agreement consisted of the following (in thousands):

	Year Ended December 31,		
	2012	2013	2014
License and Services revenue	$1,538	$415	$29

The Company has determined that the regulatory milestones and commercialization royalty are contingent revenue that will be allocated to the two units of accounting (License and Services) described above, rather than recognized immediately upon satisfaction of the milestone, as they do not meet the definition of a milestone as described in the applicable accounting literature. Certain regulatory milestones do not require performance by the Company to be achieved. The payments the Company would receive for the remaining regulatory milestones are not commensurate with the performance by the Company to achieve such milestones.

6. Loan and Security Agreement

In October 2011, the Company entered into a loan and security agreement (the “Loan and Security Agreement”) with a financial institution that provided for the Company to borrow $3,000,000. Upon the drawdown of the $3,000,000, the Company issued a warrant to purchase 21,739 shares of Series B convertible preferred stock. The fair value of the warrant of $34,000 was recorded as a debt discount and is included as a reduction of loans payable on the accompanying balance sheets. The discount is amortized using the effective interest method over the life of the loan. Interest only payments were required through July 2012, and the principal amount of the loan was repayable in thirty-six equal monthly installments plus accrued interest beginning August 2012. The interest rate on the loan was 5.15% per annum. The final balloon interest payment is $270,000 and is accreted over the life of the loan. In addition, Loan and Security Agreement allowed the Company to borrow another $2,000,000, if the Company presents evidence satisfactory to the financial institution that the Company has obtained pivotal trial guidance from the FDA. The Loan and Security Agreement is collateralized by the personal property of the Company but excludes the intellectual property of the Company.

In July 2012, the Loan and Security Agreement was amended to extend the commitment period for the additional $2,000,000 loan to November 2012, and the amendment noted that the pivotal trial conditions had been satisfied. The Company did not draw on the second term loan for $2,000,000. The Company issued a warrant to purchase 14,493 shares of Series B convertible preferred stock. The fair value of the warrant of $18,000 was recorded as other assets in the accompanying balance sheets and amortized over the access period of the loan. This amount was expensed to interest expense during 2012 when the access period ended. No other provisions were changed by this amendment. The amendment was accounted for as a modification of the loan payable and the unamortized debt discount as of the date of the modification will be amortized over the new loan period, using the effective interest rate method.

In February 2013, the Loan and Security Agreement was amended to provide for a new loan of $3,000,000 and repayment of the outstanding principal of the original loan entered into October 2011, with the remaining proceeds provided to the Company. The Company amended a warrant to purchase 8,316 shares of Series B convertible preferred stock. The fair value of this warrant of $10,500 was recorded as other assets in the accompanying balance sheets and amortized over the access period of the loan. This amount was expensed to interest expense during 2013 when the access period ended. Additionally, the Company issued a separate warrant to purchase 24,946 shares of Series B convertible preferred stock. The fair value of the warrant of $32,000 was recorded as a debt discount and is included as a reduction of loans payable in the accompanying balance sheets.

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The interest rate is 3.25% per annum and the loan is repayable in thirty equal monthly installments, following a ten-month interest only period. The final balloon interest payment is $345,000 and is accreted over the life of the loan. Additionally, the amendment provided the terms for a second loan for $1,250,000 that would be available through November 2013, contingent on satisfying a clinical trial milestone. The amendment was accounted for as a modification of loans payable, and the unamortized debt discount as of the date of the modification will be amortized over the new loan period, using the effective interest rate method.

In December 2013, the Loan and Security Agreement was again amended to extend the commitment date for the second loan of $1,250,000 to January 31, 2014. The amendment extended the interest only period for four additional months and reduced the number of payments to twenty-nine equal monthly installments if the new loan is drawn. The amendment was accounted for as a modification of the loans payable, and the unamortized debt discount as of the date of the modification will be amortized over the new payment period, using the effective interest rate method.

In January 2014, the Company drew the second loan of $1,250,000. The Company issued a warrant to purchase 10,394 shares of Series B convertible preferred stock. The fair value of the warrant of $20,000 was recorded as a debt discount and is included as a reduction of loans payable in the accompanying balance sheets. The discount is amortized using the effective interest method over the life of the loan. The interest rate is 3.59% per annum and the loan is repayable in twenty-nine equal monthly installments, following a three-month interest only period. The final balloon interest payment is $144,000 and is accreted over the life of the loan.

In September 2014, the Loan and Security Agreement was amended to provide for a new loan of $4,500,000 and repayment of the outstanding principal of the loan amounts disbursed in February 2013 and January 2014, with the remaining proceeds provided to the Company. The Company issued a warrant to purchase 18,709 shares of Series B convertible preferred stock. The fair value of this warrant of $83,000 was recorded as a debt discount and is included as a reduction of loans payable in the accompanying balance sheets. The discount is amortized using the effective interest method over the life of the loan. The interest rate is 3.95% per annum and the loan is repayable in thirty-six equal monthly installments, following a nine-month interest only period. The final balloon interest payment is $517,500 and is accreted over the life of the loan. Additionally, the amendment provided for an extension of the interest only period to a eighteen-month period if certain financing events or a combination of clinical trial and financing events occur. The amendment was accounted for as a modification of loans payable, and the unamortized debt discount as of the date of the modification will be amortized over the new loan period, using the effective interest rate method.

The Loan and Security Agreement contains customary representations and warranties, covenants, closing and advancing conditions, events of defaults and termination provisions. The Loan and Security Agreement provides that an event of default will occur if (1) the financial institution determines that it is the clear intention of the Company’s investors to not continue to fund the Company in the amounts and timeframe necessary to enable the Company to satisfy the Company’s financial obligations, (2) there is a material impairment in the financial institution’s security interest in the personal property that is the collateral, (3) the Company defaults in the payment of any amount payable under the agreement when due or (4) the Company breaches any negative covenant or certain affirmative covenants in the agreement (subject to a grace period in certain cases). The repayment of the loan is accelerated following the occurrence of an event of default or otherwise, which would require the Company to immediately pay an amount equal to: (i) all outstanding principal plus accrued but unpaid interest, (ii) the final payment, plus (iii) all other sums, that shall have become due and payable but have not been paid, including interest at the default rate with respect to any past due amounts. As of December 31, 2014, the Company was in compliance with all the covenants in the Loan and Security Agreement.

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As disclosed in footnote 1, there is substantial doubt about the Company's ability to continue as a going concern. If, in fact, the Company is unable to meet its payment obligations under the Loan and Security Agreement during the twelve months following the balance sheet date, the lender may choose to accelerate repayment under the definition of the event of default provisions and, as such, the loans payable are classified as a current liability on the accompanying balance sheet.

Aggregated annual payments due under the Loan and Security Agreement are as follows:

As of December 31, 2014 (in thousands)	
2015	$1,005
2016	1,595
2017	1,595
2018	1,181
Total payments	5,376
Less: Interest	(876)
Present value of loans payable	4,500
Less: Debt discount	(114)
Add: Final payment	517
Less: Unamoritzed portion of final payment	(468)
Loans payable	$4,435

7. Convertible Promissory Notes

On September 29, 2014, the Company entered into a convertible note purchase agreement and issued convertible promissory notes (the "Notes") in an aggregate principal amount of $5.0 million to several related parties that own more than 10% of the Company's capital. Upon completion of an initial public offering, the Notes will automatically convert into a number of shares of the Company's common stock equal to the quotient obtained by dividing the entire principal amount and accrued interest on the Notes by 80% of the initial public offering price per share of the Company's common stock. If the Company, prior to the completion of an initial public offering, issues a next series equity financing with proceeds of at least $10,000,000, excluding conversion of the Notes, the Notes will automatically convert into the shares of the next equity series. The number of shares of the Company's common stock at this conversion will be equal to the quotient obtained by dividing the entire principal amount and accrued interest on the Notes by 80% of the next equity series financing price per share. In the event that the Company does not complete an initial public offering or a next series equity financing on or before June 30, 2015, if holders of at least a majority of the principal amount of the then-outstanding Notes elect to convert the Notes, rather than electing to have the Notes repaid in cash following the maturity date of December 31, 2015, the conversion must be in to shares of the Series B convertible preferred stock.

In the event that the Company sells or disposes of all or substantially all of its property or business or merges or consolidates with any other entity (other than its wholly-owned subsidiary) prior to the repayment or conversion of the Notes, holders of the Notes will be paid an amount equal to 120% of the outstanding principal amount, together with any accrued interest, so long as the Company's indebtedness under the Loan and Security Agreement has been paid in full.

The Notes bear interest at a rate of 5% per annum, compounded annually. Unless converted, the Notes will mature upon the demand by holders of at least a majority of the principal amount of the then-outstanding notes at

any time on or after December 31, 2015, but in no event before the Company's indebtedness under the Loan and Security Agreement has been paid in full.

Due to the automatic conversion features contained in the Notes, the actual number of shares of common stock or preferred stock that would be required if a conversion of the Notes was made through the issuance of the Company's common or preferred stock cannot be predicted. In addition, the conversion that occurs upon a change in control of the Company meets the definition of a put option and is not closely related to the debt. As a result, the automatic conversion features and put option, exclusive of the Series B conversion feature as described in previous paragraphs, require derivative accounting treatment and will be bifurcated from the Notes and marked to market each reporting period through the statement of operations and comprehensive loss. The fair value of the automatic conversion features and put option of the Notes, exclusive of the Series B conversion feature as described in previous paragraphs, was recorded as a derivative liability instrument that will be measured at fair value at each reporting period. The Company estimated the fair value of the derivative by estimating the fair value of the Notes with and without the conversion derivative. To calculate the fair value of the Notes without the conversion derivative, the Company estimated the present value of the expected cash payments at an assumed discount rate of 8.25%. To calculate the fair value of the Notes with the conversion feature, the Company calculated the present value of the Notes upon conversion at an initial public offering, and the present value of the Notes at an equity financing. The risk-free rate for the assumed discount period is estimated at .05% and .15% in the respective conversion scenarios. The risk-free rate for the assumed discount period is estimated at .05% and .12% in the respective conversion scenarios at the valuation date of December 31, 2014. The Company applied a probability of occurrence to all of the conversion scenarios and estimated a weighted value of the Notes with the conversion feature. The difference between the fair value of the Notes with and without the conversion features is the derivative. The fair value of the derivative at the date of issuance is $1,067,000. The fair value of the derivative at December 31, 2014 is $1,495,000.

The Company determined that the Notes contain a beneficial conversion feature related to the conversion feature of the Notes into Series B convertible preferred stock. The beneficial conversion feature results from the difference between the fair value of the Company's common stock at the date of issuance and the Series B Preferred Stock Conversion price of $4.8104 at the date of issuance. The beneficial conversion feature is $2,275,000 as of the date of issuance and is recorded as a debt discount that will be amortized until the Note maturity date. Any changes in the beneficial conversion amount at the date of an actual conversion will be recorded at that time.

8. Convertible Preferred Stock

Convertible preferred stock as of December 31, 2012 consisted of the following (in thousands, except share data):

Series	Shares		Liquidation Amount	Proceeds Net of Issuance Costs
	Authorized	Outstanding		
A	6,574,364	1,611,089	$ 7,750	$ 7,595
B	27,796,941	5,404,948	26,000	25,951
	34,371,305	7,016,037	$ 33,750	$33,546

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Convertible preferred stock as of December 31, 2013 and December 31, 2014 consisted of the following (in thousands, except share data):

Series	Shares		Liquidation Amount	Proceeds Net of Issuance Costs
	Authorized	Outstanding		
A	6,574,364	1,611,089	$ 7,750	$ 7,595
B	27,796,941	6,657,442	32,025	31,961
	34,371,305	8,268,531	$ 39,775	$39,556

The rights, privileges and preferences of convertible preferred stock are as follows:

Dividends

The holders of the Series A and Series B convertible preferred stock are entitled to receive noncumulative annual dividends at the rate of 8% of the original issuance price, or approximately $0.38 per share, respectively, when, as and if declared by the Board of Directors. Dividends on preferred stock shall be payable in preference to and prior to payment of dividends on common stock. In the event that dividends are paid on common stock, an additional dividend shall be paid on preferred stock in an amount equal per share (on an as-if-converted basis) to the amount paid for each share of common stock. No dividends have been declared from inception to December 31, 2014.

Liquidation Rights

In the event of any liquidation, dissolution or winding up of the Company, the holders of the Company's convertible preferred stock shall be entitled to receive, prior to any distribution of the Company's assets to the holders of common stock, an amount equal to $4.8104 per share for each outstanding share of Series A and Series B convertible preferred stock, plus any declared but unpaid dividends. If the Company's assets shall be insufficient to provide for such preferential distributions, the preferred stockholders shall be entitled to pro rata distributions. The remaining assets of the Company shall be distributed among the preferred stockholders and the common stockholders pro rata on an as-if-converted basis until the holders of Series A and Series B preferred stock have received an aggregate of $14.43 per share, respectively. Thereafter, if assets remain in the Company, the common stockholders shall receive all of the Company's remaining assets on a pro rata basis. A sale of all or substantially all of the assets of the Company, merger or consolidation, which result in the Company's stockholders immediately prior to such transaction not holding at least 50% of the voting power of the surviving, continuing or purchasing entity shall be deemed a liquidation of the Company.

Due to the liquidation rights in a deemed liquidation, the Company's convertible preferred stock is classified outside of permanent equity (deficit) as mezzanine.

Modification of Series B Convertible Preferred Stock

In December 2012, the Company approved the adjustment of the Series B convertible preferred stock liquidation preference from $5.52 per share to $4.8104 per share. In order to preserve the aggregate liquidation preference of the Series B convertible preferred stockholders at that time, the Company issued 534,467 shares of Series B convertible preferred stock to such holders. As part of this analysis, the Company assessed the economic

characteristics and risks of its convertible preferred stock, including conversion, liquidation and redemption features, as well as dividend and voting rights. Based on the Company's determination that each series of its convertible preferred stock is an "equity host," the Company determined that the features of the convertible preferred stock are most closely associated with an equity host and, although the convertible preferred stock includes conversion features, such conversion features do not require bifurcation as a derivative liability. The Company also determined that the conversion option with a contingent reduction in the conversion price, upon occurrence of certain dilutive events, is a potential contingent beneficial conversion feature. In accordance with certain antidilution provisions contained in the Series B convertible preferred stock agreements, issuances of Series B convertible preferred stock in 2012 resulted in an antidilution adjustment of the conversion prices for the Series B convertible preferred stock during the year ended December 31, 2012. As a result, the Company performed a calculation to determine if a beneficial conversion feature was triggered for the Series B convertible preferred stock at each issuance of Series B in 2012. The fair value of common stock, as determined by management and the Board of Directors, on the corresponding issuance dates of Series B convertible preferred stock in each instance was below the adjusted accounting conversion prices. Therefore, no beneficial conversion feature was identified. The Company will continue to evaluate if a beneficial conversion feature needs to be recorded upon each subsequent adjustment of the conversion price based upon the difference between the adjusted conversion price and the fair market value of common stock at the original issuance date. This change is treated as a modification of the Series B preferences and results in a deemed dividend of Series B convertible preferred stock of $111,000. This amount is recorded as a reduction of additional paid-in-capital and an increase in the Series B convertible preferred stock in the accompanying financial statements.

Conversion Rights

The Company's preferred stock is convertible, at the option of the holder, into common stock on a one-for-one basis with the conversion ratio subject to adjustment in the event of certain dilutive stock issuances or other future events. Conversion is automatic upon the closing of a firm commitment underwritten public offering in which the aggregate gross proceeds equals or exceeds $30,000,000, or the date specified by written agreement of the holders of at least two-thirds of the preferred stock then issued and outstanding on an as-if-converted basis.

Voting Rights

The holder of each share of the Company's convertible preferred stock has the right to one vote for each share of common stock into which such convertible preferred stock could be converted. The holders of Series A convertible preferred stock and series B convertible preferred stock, voting as separate classes, are entitled to elect two members each of the Board of Directors, and the holders of common stock, voting as a separate class, are entitled to elect one member of the Board of Directors. The holders of common stock and preferred stock, voting together as a single class on an as-if-converted basis, are entitled to elect all remaining members of the Board of Directors.

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9. Convertible Preferred Stock Warrants

The Company issued warrants to purchase shares of the Company's convertible preferred stock at various times between the years ended December 31, 2004 and 2014 in connection with loans payable. The convertible preferred stock warrants outstanding as of December 31, 2012, 2013 and 2014 were issued as follows:

Series A Warrant

During 2006, the Company issued a warrant to purchase a total of which is exercisable for 20,788 shares of Series A convertible preferred stock, with an exercise price of $4.8104 per share and a contractual term of 10 years. The fair value of the warrant of $79,000 was recorded as a warrant liability upon issuance.

Series B Warrants

In October 2011, the Company issued a warrant to purchase 21,739 shares of Series B convertible preferred stock in connection with the Loan and Security Agreement. This warrant originally had an exercise price of $5.52 per share. The fair value of the warrant issued in the amount of $34,000 was recorded as a warrant liability upon issuance. The Company estimated the fair value of the preferred stock warrant liability by using the backsolve method to determine an enterprise value of the Company. The Black-Scholes option-pricing model was used to allocate the value of the Company to the warrant, with the following assumptions: a time to liquidity event of 5 years, 65.0% expected volatility, 0.83% risk-free interest rate and no expected dividend.

In July 2012, the Company issued a warrant to purchase 14,493 shares of Series B convertible preferred stock at $5.52 per share in connection with the modification of the Loan and Security Agreement. The fair value of the warrant issued in the amount of $18,000 was recorded as a warrant liability upon issuance. The Company estimated the fair value of the preferred stock warrant liability by using the backsolve method to determine an enterprise value of the Company. The Black-Scholes option-pricing model was used to allocate the value of the Company to the warrants, with the following assumptions: a time to liquidity event of 4 years, 65.0% expected volatility, 0.50% risk-free interest rate and no expected dividend.

In December 2012, the Company issued a warrant to purchase 5,344 shares of Series B convertible preferred stock at $4.8104 per share in connection with the reduction in the liquidation price of the Series B convertible preferred stock previously discussed. The warrant was issued to maintain the aggregate liquidation preferences. The fair value of the warrant issued in the amount of $6,700 was recorded as a warrant liability upon issuance. The Company estimated the fair value of the preferred stock warrant liability by using the backsolve method to determine an enterprise value of the Company. The Black-Scholes option-pricing model was used to allocate the value of the Company to the warrants, with the following assumptions: a time to liquidity event of 4 years, 60.0% expected volatility, 0.54% risk-free interest rate and no expected dividend. In connection with the reduction in liquidation preference of Series B convertible preferred shares the Company decreased the liquidation preference of the Series B warrants to $4.8104.

In February 2013, the Company issued a warrant to purchase 33,262 shares of Series B convertible preferred stock in connection with the modification of the Loan and Security Agreement. The warrant has an exercise price of $4.8104 per share. The fair value of the warrant issued in the amount of $31,500 was recorded as a warrant liability upon issuance. The Company estimated the fair value of the preferred stock warrant liability for the February 2013 warrants by using the backsolve method to determine an enterprise value of the Company. The Black-Scholes option-pricing model was used to allocate the value of the Company to the warrants, with the following assumptions: a time to liquidity event of 4 years, 60.0% expected volatility, 0.54% risk-free interest rate and no expected dividends.

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In January 2014, in connection with the second draw down under the Loan and Security Agreement the Company issued a warrant to purchase 10,394 shares of Series B convertible preferred stock. The warrant has an exercise price of $4.8104 per share and a contractual term of ten years from issuance. The fair value of the warrant issued in the amount of $19,000 was recorded as a warrant liability upon issuance. The Company estimated the fair value of the preferred stock warrant liability by calculating the enterprise value by applying a probability of two scenarios, going public or remaining private. To allocate the enterprise value, the Company used the current value method in the scenario of going public or being acquired with the assumption of a going public return rate of 30%. The Company used the Black-Scholes option-pricing method to allocate the enterprise value for remaining private in the near to mid-term with the following assumptions: a time to liquidity event of 3 years, 60.0% expected volatility, 0.78% risk-free interest rate and no expected dividend.

In September 2014, in connection with the amendment to the Loan and Security Agreement, the Company issued a warrant to purchase 18,709 shares of Series B convertible preferred stock. The warrant has an exercise price of $4.8104 per share and a contractual term of ten years from issuance. The fair value of the warrant issued in the amount of $83,000 was recorded as a warrant liability upon issuance. The Company estimated the fair value of the preferred stock warrant liability by calculating the enterprise value and applying a probability of two scenarios, going public or remaining private. To allocate the enterprise value, the Company used the current value method in the scenario of going public or being acquired with the assumption of a going public return rate of 30%. The Company used the Black-Scholes option-pricing method to allocate the enterprise value for remaining private in the near to mid-term with the following assumptions: a time to liquidity event of 3 years, 55.0% expected volatility, 1.07% risk-free interest rate and no expected dividend.

As of December 31, 2012, 2013 and 2014, the following convertible preferred stock warrants were outstanding (in thousands, except share and per share amounts):

	Number of Shares Underlying Warrants	Exercise Price per Share	Fair Value, as of December 31, 2012
Series A preferred stock	20,788	$4.8104	$ 26
Series B preferred stock	41,576	4.8104	53
Total	62,364		$ 79

	Number of Shares Underlying Warrants	Exercise Price per Share	Fair Value, as of December 31, 2013
Series A preferred stock	20,788	$4.8104	$ 40
Series B preferred stock	74,838	4.8104	144
Total	95,626		$ 184

	Number of Shares Underlying Warrants	Exercise Price per Share	Fair Value, as of December 31, 2014
Series A preferred stock	20,788	$4.8104	$ 46
Series B preferred stock	103,941	4.8104	417
Total	124,729		$ 463

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The fair value of the convertible preferred stock warrant liability was remeasured as of each period end. As of December 31, 2012, the Company remeasured the fair value by using the backsolve method to determine an enterprise value of the Company. The Black-Scholes option-pricing model was used to allocate the value of the Company to the warrants, with the following assumptions: a time to liquidity event of 4 years, 60.0% expected volatility, 0.54% risk-free interest rate and no expected dividend. As of December 31, 2013, the Company remeasured the fair value by calculating the enterprise value by applying a probability of two scenarios, going public or remaining private. To allocate the enterprise value, the Company used the current value method in the scenario of going public. In the scenario of remaining private, the Company used the Black-Scholes option-pricing method to allocate the enterprise value with the following assumptions: a time to liquidity event of 3 years, 60.0% expected volatility, respectively, 0.78% risk-free interest rate, respectively and no expected dividend. As of December 31, 2014, the Company remeasured the fair of the convertible preferred stock warrant liability using a Black-Scholes option-pricing method with the following assumptions: a weighted average remaining life of 6.7 years, an expected volatility of 58.9%, a weighted average risk-free interest rate of 1.80% and no expected dividend. The Company evaluated the down-round protection provisions of the warrant agreements by using a Monte Carlo simulation model and determined that the impact of such provisions was immaterial to the fair value of the warrants at the reporting dates. The assumptions are further described as follows:

Expected Time to liquidity event — The Company estimated the time to liquidity event based on management's analysis of the business, market conditions and clinical development.

Expected Volatility — The Company estimates the expected volatility based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected time to liquidity event. When selecting the publicly traded biopharmaceutical companies, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the time to liquidity event. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Risk-Free Interest Rate — The risk-free interest rate is based on U.S. Treasury zero-coupon issues with remaining terms similar to the expected time to the liquidity event.

Expected Dividend Rate — The Company has never paid any dividends and does not plan to pay dividends in the foreseeable future, and, therefore, used an expected dividend rate of zero in the valuation model.

10. Common Stock

The Company's Amended and Restated Certificate of Incorporation, as amended, has authorized 45,000,000 shares of common stock at $0.001 par value.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the board of directors, if any, subject to the preferential dividend rights of the holders of the Series A and B convertible preferred stock. As of December 31, 2014, no dividends have been declared.

During 2004, the Company issued a warrant to purchase 1,203 shares of common stock to an investor. The warrant had an exercise price of $0.004 per share and a contractual term of ten years from issuance. The warrant expired in March 2014 and was never exercised. The fair value of the warrant was immaterial.

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11. 401 (K) Plan

The Company sponsors a 401(k) Plan that stipulates that eligible employees can elect to contribute to the 401(k) Plan, subject to certain limitations, on a pretax basis. Pursuant to the 401(k) Plan, the Company does not match any employee contributions.

12. Stock Option Plan

2004 Stock Incentive Plan

In 2004, the Board of Directors approved the 2004 Stock Incentive Plan (the 2004 Plan), which provides for the granting of incentive and non-statutory stock options to employees, directors, and consultants at the discretion of management and the Board of Directors. In December 2005, the Board of Directors authorized the number of shares available for grant under the Plan to be 239,825. In February 2006, the Board of Directors authorized an additional 62,500 shares available for grant under the Plan. In June 2007, the Board of Directors authorized an additional 20,000 shares available for grant under the Plan. In November 2007, the Board of Directors authorized an additional 625,000 shares available for grant under the Plan. In December 2012, the Board of Directors authorized an additional 564,290 shares available for grant under the Plan. In June 2013, the Board of Directors authorized an additional 173,218 shares available for grant under the Plan.

Incentive stock options are granted with exercise prices not less than the estimated fair value of common stock, and non-statutory stock options may be granted with an exercise price of not less than 100% of the estimated fair value of the common stock on the date of grant. Options granted under the Plan expire no later than 10 years from the date of grant. Incentive stock options granted under the Plan vest over periods determined by the Board of Directors, generally over four years. Non-statutory stock options vest based on the terms of the individual agreement, generally from nine months to four years.

In April 2014, the Company terminated the 2004 Plan and the Board of Directors approved the 2014 Stock Option Plan (the 2014 Plan), authorizing 250,000 shares for issuance under the 2014 Plan. Shares underlying any outstanding stock awards or stock option grants previously awarded remain subject to the terms of the 2004 Plan. Any shares available for grant or any shares canceled or forfeited prior to vesting or exercise subsequent to the termination of the 2004 Plan became available for use under the 2014 Plan. Upon the effectiveness of the 2014 Plan, the Company ceased granting any equity awards under the 2004 Plan. Subsequent awards have been and will be granted under the 2014 Plan.

Stock Option Modifications

On June 6, 2013, the Company’s Board of Directors approved the reduction of the exercise prices of certain outstanding stock options previously granted to employees of the Company who were still providing services to the Company as of that date. The Company repriced options to purchase 44,500 shares of the Company’s common stock that included both vested and unvested stock options granted in December 2010 with original exercise prices of $1.12 per share. The Company’s Board of Directors adjusted all of the original exercise prices for the repriced options to $0.56 per share. No other terms of the repriced options were modified and these repriced stock options will continue to vest according to their original vesting schedules and will retain their original expiration dates. These modifications were treated as one-for-one exchanges of the previously issued stock options for new stock options with an exercise price of $0.56 per share. The Company recorded stock-based compensation expense of $4,000 for the incremental value of the vested options. In addition, the Company

will recognize additional stock-based compensation expense of $2,400 for the incremental value of the unvested repriced options over the remaining vesting period of the replacement award.

On April 20, 2012, the Company's Board of Directors approved the extension of the post-termination exercise period for the vested options of a former consultant. The Company extended the exercise period to purchase 151,922 shares of the Company's stock from the original 90 days post-termination to one year after the end of the contract with the nonemployee. The final contract date was November 30, 2012 and the exercise period extended to November 30, 2013. The Company recorded stock-based compensation expense of $14,000 for the incremental value of the vested options.

On May 31, 2013, the Company's Board of Directors approved the extension of the post-termination exercise period to purchase 354,372 shares of the Company's stock from the original 90 days post-termination to the updated one year post-termination. The termination date was May 31, 2013 and the exercise period extended to May 31, 2014. The former employee exercised 68,602 options to purchase common stock on May 30, 2014 and the remaining 285,770 options were cancelled. The Company recorded stock-based compensation expense of $34,000 for the incremental value of the vested options.

On August 29, 2013, the Company's Board of Directors approved a second extension of the post-termination exercise period for the vested options of a former consultant. The exercise period had previously been extended to November 30, 2013 as noted previously in this section. The Company extended the exercise period to purchase 151,922 shares of the Company's stock for an additional four months past the one year post-termination period. The one year post-termination date was November 30, 2013 and the exercise period extended to March 31, 2014. The Company recorded stock-based compensation expense of $4,000 for the incremental value of the vested options.

Performance Grants

In 2009, the Company granted 92,140 options to purchase shares of common stock, and 63,750 of those options granted to certain employees contained a performance based vesting condition. 31,875 of those options vested immediately, and 31,875 of the options vest contingently upon the safe treatment of the first ten patients in the Company's Phase 2b trial known as COR1.0 The grant date fair value of the performance options was $19,000. In March 2013, 127,500 options were deemed to be vested and expense of $19,000 was recognized. No expense had been recognized previously related to these options as the performance conditions were not considered probable of achievement prior to that date.

In 2010, the Company granted 240,750 options to purchase shares of common stock, and 150,000 of those options granted to certain employees and nonemployees contained a performance based vesting condition. The options will vest upon (1) a sale/merger of the Company including a carveout transaction; (2) an up-front investment or payment from a corporate partner together with an option to purchase the Company; (3) an equity investment by a corporate partner in the Company Series C financing in an amount equal to or greater than 25% of the total funds raised in the round. In April 2013, 95,000 shares of unvested performance options were cancelled as the performance condition was not met and 55,000 shares of unvested performance options were cancelled in November 2012 due to employee termination. No expense was recognized previously in any reporting period related to these options as the performance conditions were not considered probable of achievement at any date.

In 2013, the Company granted 1,038,473 options to purchase shares of common stock, and 207,362 of those options granted to certain employees contained a performance based vesting condition. Standard monthly vesting

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commenced for 103,681 of the options upon the successful recruitment of a specific number of patient subjects in the Company's COR1.1 clinical study. The grant date fair value of the performance options was $120,000. The performance based vesting condition commenced on September 30, 2014. Expense of $3,000 was recognized for the year ended December 31, 2014, and the performance options will continue to vest over the remaining vesting period. The remaining 103,681 options vest over a 48 month period.

The following table summarizes the activity under the Company's Plan (in thousands, except share and per share amounts):

		Options Issued and Outstanding			
	Shares Available for Grant	Number of Shares	Weighted Average Exercise Price	Remaining Contractual Life (in years)	Aggregate Intrinsic Value
Balance at December 31, 2012	684,196	897,520	$ 1.04	5.38	
Increase in shares reserved for issuance	173,217				
Options granted	(1,038,473)	1,038,473	$ 0.56		
Options exercised		(21,254)	$ 0.80		
Options cancelled	264,617	(264,617)	$ 0.88		
Balance at December 31, 2013	83,557	1,650,122	$ 0.77	6.91	
Increase in shares reserved for issuance	250,000				
Options granted	(428,072)	428,072	$ 7.24		
Options exercised		(248,909)	$ 0.92		
Options cancelled	500,412	(500,412)	$ 1.52		
Balance at December 31, 2014	405,897	1,328,873	$ 2.54	7.99	$5,079,000
Vested and expected to vest at December 31, 2014		1,263,918	$ 2.46	7.92	$4,469,000
Vested at December 31, 2014		549,936	$ 0.95	6.44	$2,793,000

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The following table summarizes information concerning outstanding and exercisable options under the Plan as of:

Exercise Price	Options Outstanding and Exercisable at December 31, 2013		Options Vested and Exercisable at December 31, 2013	
	Number Outstanding	Weighted Average Remaining Contractual Life (in Years)	Number Outstanding	Weighted Average Remaining Contractual Life (in Years)
$ 0.56	927,409	9.24	95,325	8.42
$ 0.80	233,374	2.11	224,588	2.11
$ 0.96	89,639	5.95	89,640	5.95
$ 1.00	26,500	3.61	26,500	3.61
$ 1.12	31,700	7.00	31,700	7.00
$ 1.20	341,500	4.38	341,500	4.38
	1,650,122	6.91	809,253	4.48

Exercise Price	Options Outstanding and Exercisable at December 31, 2014 (unaudited)		Options Vested and Exercisable at December 31, 2014 (unaudited)	
	Number Outstanding	Weighted Average Remaining Contractual Life (in Years)	Number Outstanding	Weighted Average Remaining Contractual Life (in Years)
$ 0.56	748,840	8.25	328,564	8.06
$ 0.80	24,432	1.13	24,432	1.13
$ 0.96	56,764	4.95	56,764	4.95
$ 1.00	26,500	2.61	26,500	2.61
$ 1.12	6,700	5.98	6,700	5.98
$ 1.20	89,000	3.38	89,000	3.38
$ 7.00	289,270	9.84	17,976	9.84
$ 8.20	87,367	9.99	—	—
	1,328,873	7.99	549,936	6.44

The intrinsic value of options exercised was $0, $35,000 and $1,015,000 for the years ended December 31, 2012, 2013 and 2014. The intrinsic value was calculated as the difference between the exercise price of the options and the estimated fair value of the Company's common stock at those reporting dates.

The total estimated grant date fair value of options vested during the years ended December 31, 2012, 2013 and 2014 was $34,000, $103,000, and $343,000, respectively.

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Stock-Based Compensation

Total stock-based compensation recognized was as follows (in thousands):

	Year Ended December 31,		
	2012	2013	2014
Research and Development	$ 13	$ 45	$ 171
General and administrative	34	193	210
Total	$ 47	$ 238	$ 381

At December 31, 2014, there was $1,069,000 of unrecognized stock-based compensation expense, net of estimated forfeitures, related to unvested share options with a weighted-average remaining recognition period of 3.11 years. The non-employee stock-based compensation expense was not material for all periods presented.

In determining the fair value of the stock-based awards, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected Term — The Company's expected term represents the period that the Company's stock-based awards are expected to be outstanding. The Company used the average of the expected term as disclosed for comparable publicly traded biopharmaceutical companies since the Company does not have sufficient experience to estimate the expected term based on historical exercises. The expected term of stock options granted to non-employees is equal to the contractual term of the option award.

Expected Volatility — Since the Company is privately held and does not have any trading history for its common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. When selecting comparable publicly traded biopharmaceutical companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Risk-Free Interest Rate — The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend — The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

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The fair value of stock option awards to employees was estimated at the date of grant using a Black-Scholes option-pricing model with the following weighted-average assumptions:

	Year Ended December 31,		
	2012	2013	2014
Expected term (in years)	N/A	5.39	5.39
Expected Volatility	N/A	80.7%	56%
Risk-free interest rate	N/A	0.87 to 1.47%	1.70 to 1.82%
Dividend yield	N/A	0%	0%

The weighted-average, estimated grant-date fair value of employee stock options granted during the years ended December 31, 2012, 2013 and 2014 was zero, $0.29 and $5.10 per share, respectively.

13. Income Taxes

Since inception, the Company has generated losses from operations. The Company did not record a benefit from the income taxes for those losses during the years ended December 31, 2012, 2013 and 2014, respectively, due to its uncertainty of realizing a benefit from those losses.

The components of the income tax expense are as follows (in thousands):

	Years ended December 31,		
	2012	2013	2014
Current income tax expense:			
State	$—	$—	$—
Deferred income tax benefit:			
State	—	—	—
Total income tax expense	$—	$—	$—

Income tax expense in 2012, 2013 and 2014 differed from the amount expected by applying the statutory federal tax rate to the loss before taxes as summarized below:

	December 31,		
	2012	2013	2014
Federal tax benefit at statutory rate	34%	34%	34%
Change in valuation allowance	(34)	(35)%	(36)%
Research and development credits	—	3%	1%
Non-deductible expenses and other	—	(2)%	1%
Total	0%	0%	0%

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Significant components of the Company's net deferred tax assets as of December 31, 2012, 2013 and 2014 consist of the following (in thousands):

	December 31,		
	2012	2013	2014
Deferred tax assets			
Net operating loss carryforwards	$ 11,120	$ 13,211	$ 17,439
Accruals and reserves	50	96	910
Stock based compensation	61	80	59
Research and development credit carryforwards	685	873	1,016
Property and equipment	4	5	3
	11,920	14,265	19,427
Less: Valuation allowance	(11,920)	(14,265)	(18,243)
Deferred tax assets, net of valuation allowance	—	—	1,184
Convertible promissory notes discount	—	—	(1,168)
Fixed assets	—	—	(16)
Net deferred tax assets (liabilities)	$ 0	$ 0	$ 0

The Company has established a full valuation allowance against its deferred tax assets due to the uncertainty surrounding realization of these assets.

Realization of deferred tax assets is dependent on future earnings, if any, the timing and amount of which are uncertain. Accordingly, the deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $846,000, $2,345,000 and $3,978,000 for the years ended December 31, 2012, 2013 and 2014, respectively.

The Company's deferred tax assets do not include the excess tax benefit related to stock-based compensation that are a component of its federal and state net operating loss carryforwards in the amount of $0.3 million as of December 31, 2014. The excess tax benefit reflected in the Company's net operating loss carryforwards will be accounted for as a credit to additional paid-in capital within stockholders' equity, if and when realized. In determining if and when excess tax benefits have been realized, the Company has elected to utilize the with-and-without approach with respect to such excess tax benefits. The Company has also elected to ignore the indirect tax effects of stock-based compensation deductions for financial and accounting reporting purposes, and specifically to recognize the full effect of the research tax credit in income from operations.

At December 31, 2014, the Company had net operating loss ("NOL") carryforwards for federal income tax purposes of approximately $44,169,000 that expire beginning in 2024 if not utilized, and federal research and development tax credit carryforwards of approximately $629,000 that expire beginning in 2026 if not utilized. In addition, the Company had NOL carryforwards for state income tax purposes of approximately $43,777,000 that expire beginning in 2026 if not utilized, and state research and development tax credit carryforwards of approximately $586,000, which do not expire.

Utilization of the NOL and tax credit carryforwards may be subject to substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code and similar state provisions. Such an annual limitation could result in the expiration of the NOL and tax credit carryforwards before their utilization. In general, if the Company experiences a greater than 50 percentage point aggregate change (by value) in the equity

ownership of certain stockholders over a rolling three-year period (a Section 382 ownership change), utilization of its pre-change NOL carryforwards are subject to an annual limitation under Section 382 of the Internal Revenue Code (California has similar laws). Such limitations may result in expiration of a portion of the NOL carryforwards before utilization. The Company has determined that an ownership change occurred in December 2005, which resulted in a permanent loss of $287,000 of the federal net operating loss carryforwards. The ability of the Company to use its remaining NOL carryforwards may be further limited if the Company experiences a Section 382 ownership change in connection with this offering or as a result of future changes in its stock ownership.

On January 1, 2009, the Company adopted the provisions of the FASB's guidance for accounting for uncertain tax positions. The guidance prescribes a comprehensive model for the recognition, measurement, presentation and disclosure in consolidated financial statements of any uncertain tax positions that have been taken or expected to be taken on a tax return. The cumulative effect of adopting this guidance did not result in an adjustment to accumulated deficit as of January 1, 2009. It is the Company's policy to include penalties and interest expense related to income taxes as a component of other expense and interest expense as necessary. There was no interest or penalties accrued at December 31, 2012, 2013 and 2014.

At December 31, 2012, 2013 and 2014, the Company's reserve for unrecognized tax benefits is approximately $363,000, $454,000 and $521,000, respectively. Due to the full valuation allowance at December 31, 2014, current adjustments to the unrecognized tax benefit will have no impact on the Company's effective income tax rate; any adjustments made after the valuation allowance is released will have an impact on the tax rate. The Company does not anticipate any significant change in its uncertain tax positions within 12 months of this reporting date. The Company includes penalties and interest expense related to income taxes as a component of other expense and interest expense, respectively, as necessary.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	December 31,		
	2012	2013	2014
Balance at beginning of year	$339	$363	$454
Gross increases related to current year tax positions	24	69	102
Gross increases related to prior year tax positions	—	22	—
Reductions of prior year tax positions for:			
Changes in estimate			(35)
Balance at end of year	$363	$454	$521

The Company files U.S. federal and California state income tax returns with varying statutes of limitations, and currently does not have any tax audits or other proceedings pending. All tax returns will remain open for examination by the federal and state authorities for three and four years from the date of utilization of any net operating loss or credits.

14. Net Loss per Common Share and Unaudited Pro Forma Net Loss per Common Share

Basic net loss per share is calculated by dividing net loss by the weighted-average number of common shares outstanding as of January 1, 2014 or the issuance date, if later, less shares subject to repurchase, and excludes any dilutive effects of share-based awards and warrants. Diluted net loss per common share is computed giving effect to all potential dilutive common shares, including common stock issuable upon exercise of stock

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options, and unvested restricted common stock and stock units. As the Company had net losses for the years ended December 31, 2012, 2013 and 2014, all potential common shares were determined to be anti-dilutive.

The following table sets forth the computation of net loss per common share (in thousands, except per share amounts):

	Year Ended December 31,		
	2012	2013	2014
Net loss	$ (2,053)	$ (5,678)	$ (13,359)
Deemed dividend on the Series B preferred stock	(111)	—	—
Net income (loss) attributable to common stockholders, basic	(2,164)	(5,678)	(13,359)
Adjustments to net income (loss) for dilutive securities	—	—	—
Net income (loss) attributable to common stockholders, diluted	$ (2,164)	$ (5,678)	$ (13,359)
Net income (loss) per share attributable to common stockholders			
Basic and diluted	$ (5.14)	$ (13.42)	$ (21.81)
Weighted-average shares used in computing net income (loss) per share attributable to common stockholders:			
Basic and diluted	421,152	423,059	612,525

Potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows:

	As of December 31,		
	2012	2013	2014
Stock options	897,520	1,650,122	1,328,873
Convertible preferred stock	7,016,037	8,268,531	8,268,531
Convertible preferred stock warrants	62,364	95,626	124,729
Common stock warrant	1,203	1,203	1,203
Convertible promissory notes	—	—	1,052,799

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The Company has presented unaudited pro forma basic and diluted net loss per common share, which has been computed to give effect to the automatic conversion of all shares of convertible preferred stock into shares of common stock as if such conversion had occurred as of January 1, 2014 or date of issuance, if later, the conversion of preferred stock warrants into common stock warrants as of January 1, 2014 and the conversion of the outstanding principal and accrued interest on the September 2014 convertible promissory notes into common stock and the resulting loss on extinguishment of $2.5 million. The following table sets forth the computation of the Company's pro forma basic and diluted net loss per common share (in thousands, except per share amounts):

	Year Ended December 31, 2014 (unaudited)
Net loss attributable to common stockholders, basic	$ (13,359)
Change in fair value of convertible preferred stock warrant liability and derivative liability	605
Amortization of convertible promissory notes discount	410
Non-cash interest expense on convertible promissory notes	64
Loss on conversion of convertible promissory notes	(2,505)
Net loss used in computing pro forma net loss per share attributable to common stockholders, basic and diluted	$ (14,785)
Weighted-average shares used in computing net loss per share attributable to common stockholders, basic	612,525
Pro forma adjustments to reflect assumed conversion of convertible preferred stock	8,268,531
Pro forma adjustments to reflect assumed conversion of convertible promissory notes	1,266,094
Weighted-average shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted	10,147,150
Pro forma net loss per share attributable to common stockholders, basic and diluted:	$ (1.46)

15. Related Party Transactions

In November 2012, the Company entered into a technology license agreement with Shanghai Jingfeng Pharmaceutical Co., Ltd. pursuant to which the Company granted to Jingfeng an exclusive license to develop, manufacture and commercialize Hydros-TA in China, Taiwan, Hong Kong and Macau. Vivo Ventures, which is an investor in the Company with board representation, is also an investor in Jingfeng with board representation.

In December 2012 and June 2013, the Company issued 1,247,295 and 1,252,494 shares of Series B convertible preferred stock, respectively, for net cash proceeds of $6.0 million and $6.0 million, respectively. As part of this offering, 1,247,295 and 1,247,297 shares, respectively, were sold to entities owning more than 10% of our outstanding capital stock as of December 2012 and 2013.

In September 2014, the Company issued convertible promissory notes to several related parties that own more than 10% of the Company's capital stock (see Note 7).

16. Subsequent Events

For its financial statements as of December 31, 2014 and for the year then ended, the Company evaluated subsequent events through April 6, 2015, the date on which those financial statements were issued.

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On February 19, 2015, the Company entered into a convertible note purchase agreement with, and issued convertible promissory notes in an aggregate principal amount of $4.0 million to several related parties that own more than 10% of the Company's capital stock. These notes contain terms identical to those of the notes issued September 29, 2014, as described in Note 7 to these financial statements. Embedded derivatives that are required to be bifurcated from the underlying debt instrument (i.e. host) are accounted for and valued as a separate financial instrument. The Company evaluated the terms and features of the convertible promissory notes issued in February 2015 and identified embedded derivatives requiring bifurcation and accounting at fair value because the economic and contractual characteristics of the embedded derivatives met the criteria for bifurcation and separate accounting due to the conversion features (see Note 7 for a description of the conversion features).

In March 2015, the Company's board of directors and stockholders approved a 4-for-1 reverse stock split of the Company's common and preferred stock. The Company filed an amendment to its certificate of incorporation effecting the reverse stock split on March 13, 2015. The certificate of amendment also removed the "price per share" threshold for the preferred stock automatic conversion, making the conversion of preferred stock into common stock automatic either upon the closing of a firm commitment underwritten public offering in which the aggregate gross proceeds equals or exceeds $30,000,000 or upon the date specified by written agreement of the holders of at least two-thirds of the preferred stock then issued and outstanding, voting as a single class.

13,000,000 Shares

Carbylan Therapeutics, Inc.

Common Stock

PROSPECTUS

April 8, 2015

Leerink Partners

JMP Securities **Wedbush PacGrow Life Sciences**

Through and including May 3, 2015 (25 days after the commencement of this offering), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.